

STUDIES IN THE EPOXIDE-CARBONYL
REARRANGEMENT OF α -CYANO EPOXIDES

by 580

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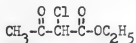
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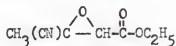
INTRODUCTION

The chemistry of α -cyano epoxides has never been reviewed extensively to date. α -Halo epoxides have been reviewed by Tabor⁵³ and Steppel⁴⁹ prior to January, 1969. These reviews mentioned some α -cyano epoxides. Mowry³⁰ had mentioned the preparation of a limited number of α -cyano epoxides in his review but only discussed the action of sodium cyanide with α -halo aldehydes and ketones.

Favrel and Provost¹³ demonstrated that the product from ethyl α -chloroacetoacetate (1) and potassium cyanide was not ethyl α -cyanoacetoacetate, but ethyl α,β -epoxy- α -cyanocrotonate (2). As shown by Kohler and Brown²³, the

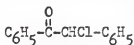


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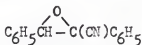


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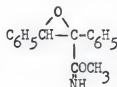
isomeric cyano epoxides, cis- (4) and trans-2,3-diphenyl-2,3-epoxypropionitrile (5) were prepared similarly from desyl chloride (3) in low yield. The cis and trans imido esters, 6, were also obtained. The formation of the



3

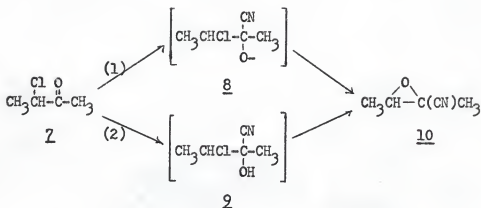


4, cis
5, trans

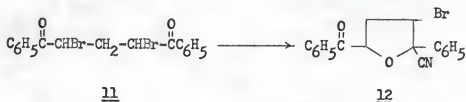


6

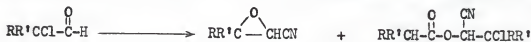
epoxide linkage is believed to occur by the attack of cyanide ion at the carbonyl carbon followed by elimination of chloride ion (path 1). α -Chloro cyanohydrin 2 has been shown not to be an intermediate in the formation of α -cyano epoxide 10.¹⁶ When the α -chloro cyanohydrin, 2, was treated with sodium cyanide, a low yield of 10 was obtained. High yields are obtained in the reaction of 7 with sodium cyanide.



2-Cyano-2-phenyl-3-bromo-5-benzoyltetrahydrofuran (12) was obtained from the reaction of 2,4-dibromo-1,5-diphenyl-1,5-pentanedione (11) with sodium cyanide.¹⁴



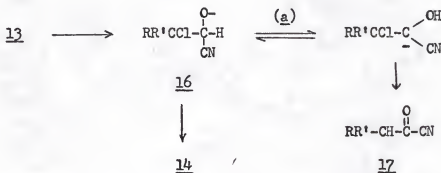
Cantacuzene and Ricard⁷ have shown that the treatment of α -chloro aldehydes with sodium cyanide results in the concurrent formation of epoxy nitrile 14 and ester 15. The products obtained depend essentially on the degree of substitution on the carbon atom adjacent to the carbonyl group. If the carbon atom bearing the chlorine is tertiary, as in 13d, only the epoxide, 14d, is obtained, while if the carbon is primary, 13a, the ester, 15a, is



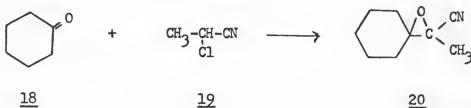
<u>13</u>	<u>14</u>	<u>15</u>
a, R=R'=H		100%
b, R=H, R'=CH ₃	17%	83%
c, R=H, R'=C ₂ H ₅	46%	54%
d, R=R'=CH ₃	100%	

obtained. If the carbon atom bearing the chlorine is secondary both products are formed.

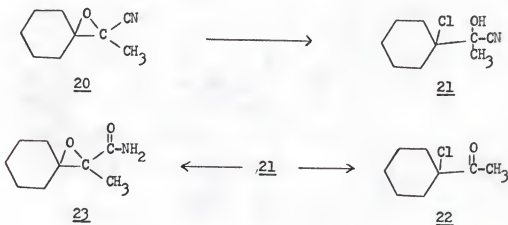
The products obtained depend on the relative acidities of the proton attached to the original carbonyl carbon atom and to the proton attached to the initial aldehyde as shown (a). The acidity of the proton is increased by the nitrile substituent which is fixed by the carbonyl group. The esters, 15, are the substitution product of the cyanohydrin alcoholate, 16, to the acyl cyanide, 17. The esters were identified by saponification which gave their respective acids.



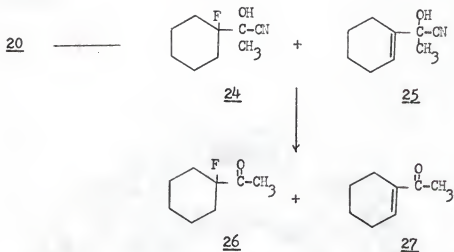
α -Cyano epoxides have also been prepared by the condensation of an aldehyde or ketone with an α -halo nitrile in the presence of potassium *tert*-butoxide,⁵⁰ sodium methoxide, or lithium amide at low temperatures.³⁸ The preparation of 2-methyl-1-oxaspiro[2.5]octane-2-carbonitrile (20) was achieved by condensing cyclohexanone (18) with α -chloropropionitrile (19) in the presence of potassium *tert*-butoxide and *tert*-butyl alcohol.⁵⁰ On the other hand, if potassium ethoxide was used as the condensing agent, an α -epoxy imido ester would also be obtained.



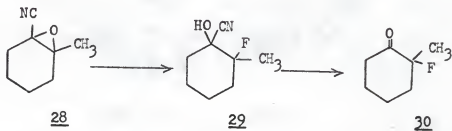
Stork⁵⁰ also studied the reactions of α -cyano epoxides with anhydrous hydrochloric acid, zinc chloride and hydrochloric acid, and borontrifluoride etherate. The reaction of 20 with anhydrous hydrochloric acid, and with zinc chloride and hydrochloric acid resulted in the formation of 2-hydroxy-2-(1-chlorocyclohexyl)propionitrile (21). The treatment of 21 with dilute sodium hydroxide for a short time (30 seconds) resulted in the isolation of 1-chlorocyclohexyl methyl ketone (22). The reaction with dilute base for several days, however, resulted in the isolation of 2-methyl-1-cxaspiro[2.5]octane-2-carboxamide (23).



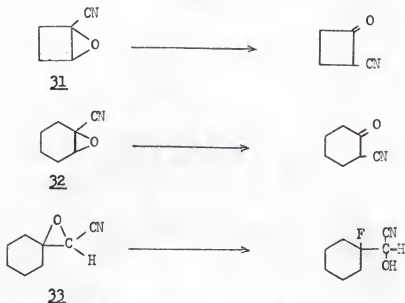
The β -fluoro cyanohydrin, 24, was also obtained when 20 was isomerized in the presence of excess borontrifluoride etherate. An unidentified product believed to be the unsaturated cyanohydrin 25 was also obtained. The products were identified by treating the cyanohydrins 24 and 25 with dilute sodium hydroxide to give α -fluoro ketone 26 and the acetyl cyclohexene (27), respectively.⁵⁰



Cantacuzene⁵ also used this procedure for the preparation of α -fluoro ketones in high yields. 2-Methyl-1-cyclohexenecarbonitrile epoxide (28) was treated with borontrifluoride etherate and hydrofluoric acid to give 1-hydroxy-2-methyl-2-fluorocyclohexanecarbonitrile (29), which was then treated with silver nitrate and one equivalent of ammonia to give 2-fluoro-2-methylcyclohexanone (30).

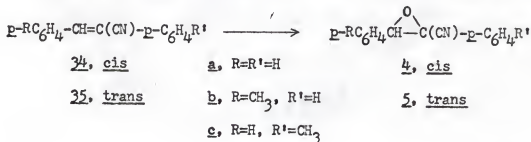


The preparation of β -fluoro cyanohydrins from various α -cyano epoxides was also attempted with hydrofluoric acid.⁴⁶ Observations showed that electron withdrawing groups inhibit epoxide ring opening reactions even in rigid systems. 1-Cyclobutenecarbonitrile epoxide (31) and 1-cyclohexenecarbonitrile epoxide (32) did not give any fluoro cyanohydrin while the rigid 1-oxaspiro[2.5]octane-2-carbonitrile (33) gave the β -fluoro cyanohydrin in low yield.



Payne and Williams³⁶ have demonstrated the preparation of α -cyano epoxides by the peroxidation of substituted acrylonitriles in the presence of base.

trans-2,3-Diphenyl-2,3-epoxypropionitrile (5a) was prepared by oxidizing trans- α -phenyl- β -p-tolylacrylonitrile (35a) with tert-butylhydroperoxide in the

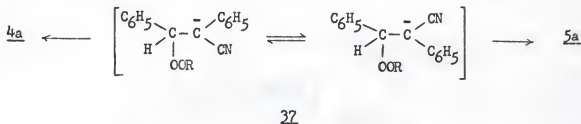


presence of benzyltrimethylammonium hydroxide (Triton B). 2,3-Dimethyl-2,3-epoxybutyronitrile (36) was prepared similarly.

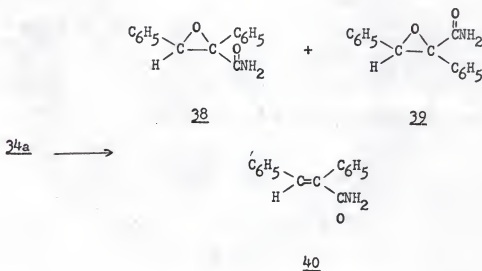


If cis- α , β -diphenylacrylonitrile (34a) is allowed to react under the same conditions, a complete reaction is observed, but no pure compound could be isolated.³⁶ Since the attack of the peroxide anion occurs at the β -carbon

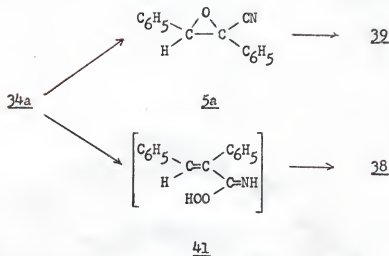
atom, as shown by Zimmerman, et al.,⁵⁸ isomerization to the most stable configuration, via 37, would result, giving a mixture of 4a and 5a.



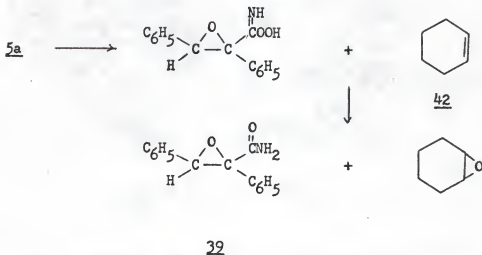
Payne and Williams³⁶ also studied the reaction of cis- α,β -diphenylacrylonitrile (34a) with alkaline hydrogen peroxide to give 38 (30%), 39 (16%), and 40 (10%).



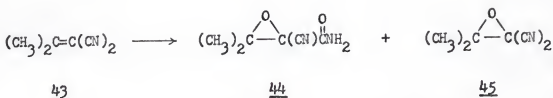
The reaction could proceed by two different reaction paths. The reaction could proceed by (1) the attack of the peroxide anion at the β -carbon atom and displacement of hydroxide ion to give the trans-2,3-diphenyl-2,3-epoxypropionitrile (5a) then hydrolyze in the presence of alkaline hydrogen peroxide to give 39, or (2) epoxidation could proceed intramolecularly by the intermediate peroxycarboximide acid (41) to give 38 since no rearrangement can occur. The authors conclude that the epoxidation must proceed predominately intramolecularly since twice as much of cis isomer 38 was isolated as of trans isomer 39.



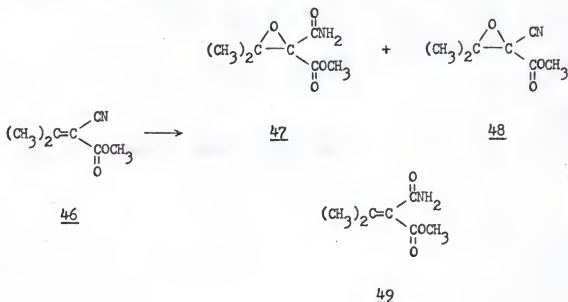
An added note in proof was that trans-epoxy amide 39 was only obtained in 30% on hydrolysis of trans-epoxy nitrile 5a with alkaline hydrogen peroxide. When cyclohexene (42) was included into the reaction system, the yield increased to 70%.



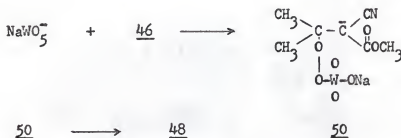
The intramolecularity of the epoxidation of acrylonitriles was shown by the epoxidation of isopropylidene malononitrile (43) with basic hydrogen peroxide.³⁴ 3-Methyl-2-cyano-2,3-epoxybutyramide (44) and 3-methyl-2,3-epoxy-2-cyanobutyronitrile (45) were obtained in a 69% and 9% yield, respectively.



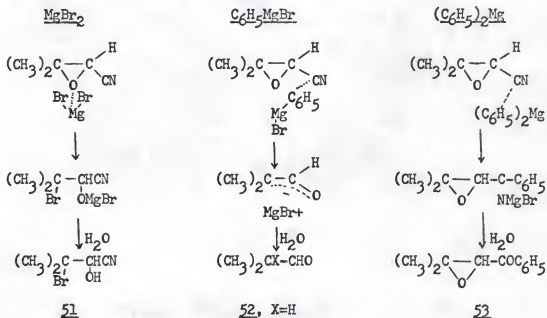
The epoxidations of alkylidene cyanoacetic esters with hydrogen peroxide in the presence of trisodium phosphate or sodium tungstate is discussed by Igarashi and Midorikawa.^{20,21} Methyl 2-cyano-3-methyl-2-butenate (46) was epoxidized in the presence of sodium tungstate to give methyl 2-carbamoyl-2,3-epoxy-3-methylbutanoate (47) along with some methyl 2-cyano-2,3-epoxy-3-methylbutanoate (48) and methyl 2-carbamoyl-3-methyl-2-butenate (49). The authors conclude that epoxy amide 47 is the product from basic hydrogen peroxide hydrolysis of epoxynitrile 48 since 48 is easily hydrolyzed under these conditions to give 47. The unsaturated amide, 49, is not epoxidized when treated with hydrogen peroxide in the presence of sodium tungstate. If a two molar equivalent of hydrogen peroxide is used in the reaction, 48 is the major product; whereas, if an excess of hydrogen peroxide is used, then 47 is obtained in high yield.



The epoxidation of alkylidene cyanoacetic esters must proceed by the attack of the pertungstate anion at the β -carbon atom since a decrease of epoxide formed is observed when increasing the bulk of the β -alkyl groups.



Cantacuzene, Ricard, and Theze⁸ have shown that electrophilic attack occurs at the oxygen of the epoxide ring, while nucleophilic attack occurs at the carbon atom of the nitrile group. The reaction of 2-methyl-2,3-epoxy-isobutanonitrile (14d) with a series of magnesium reagents were observed.



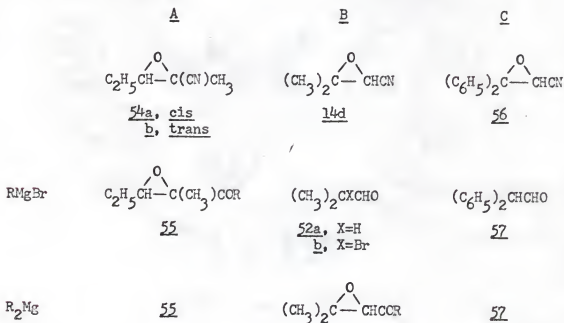
In the presence of an electrophilic reagent, MgBr_2 , the formation of the α -bromo cyanohydrin, 51, was observed; whereas, with a nucleophilic reagent, $\phi_2\text{Mg}$, the epoxy ketone (53) was obtained. When ϕMgBr was employed, which could display both nucleophilic and electrophilic properties, isobutyraldehyde (52) was the major product.

Cantacuzene and Keramat^{9,10} had shown that the epoxy nitriles which react with magnesium reagents (RMgBr , R_2Mg) can be classified into three different categories depending on the substitution on the β -carbon atom of the epoxy nitrile.

Group A compounds contain a hydrogen in the β -position of the epoxy nitrile, e.g., 54.

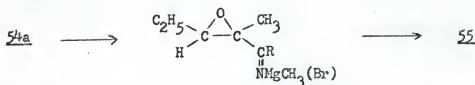
Group B compounds contain alkyl groups in the β -position of the epoxy nitrile, e.g., 14d.

Group C compounds contain aryl substituents in the β -position of the epoxy nitrile, e.g., 56.

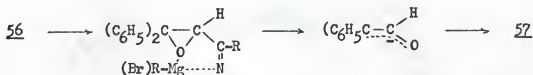


53

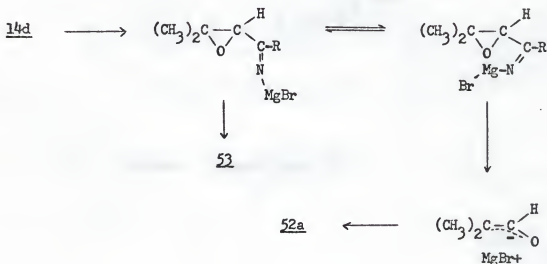
The reaction of trans-2,3-epoxypentanenitrile (54b) with $(\text{CH}_3)_2\text{Mg}$ or CH_3MgBr results in the formation of the epoxy methyl ketone (55, $\text{R}=\text{CH}_3$); the cis isomer, 54a, results in the formation of epoxy methyl ketone 55, $\text{R}=\text{CH}_3$, with $(\text{CH}_3)_2\text{Mg}$. With CH_3MgBr , 54a gives only 25% of 55 along with 75% recovered epoxide.



3,3-Diphenyl-2,3-epoxypropionitrile (56) resulted in the formation of diphenylacetaldehyde (57) with both magnesium reagents, R_2Mg and RMgBr ($\text{R}=\text{CH}_3$ or ϕ), the product of magnesium coordination with the epoxide oxygen.



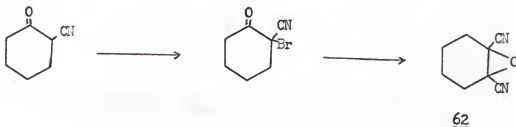
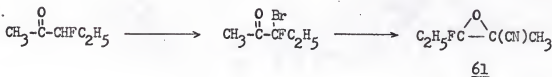
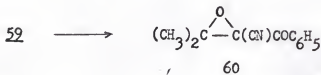
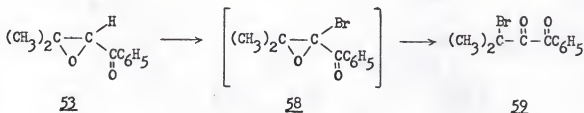
The reactions of 2-methyl-2,3-epoxybutanonitrile (14d) with ϕMgBr results in the formation of isobutyraldehyde (52a, 80%) and α -bromoisobutyraldehyde (52b, 10%); with $\phi_2\text{Mg}$, the expected product, epoxy ketone 53, $\text{R}=\text{C}_6\text{H}_5$, is obtained. Since RMgBr is more electrophilic than R_2Mg ($\text{R}=\text{CH}_3$ or ϕ) one would observe both electrophilic and nucleophilic attack on the α -cyano epoxide with ϕMgBr .



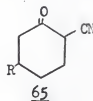
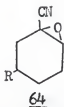
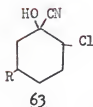
The cleavage of the beta carbon-oxygen bond, through coordination, is much more easily achieved if the substituents of the β -carbon atom are able to

donate electrons to the electron deficient center as the coordination of magnesium to oxygen occurs.

Cantacuzene⁶ has described the preparation of α -keto α -cyano epoxides. Addition of bromine to the α -keto epoxide results in the formation of intermediate 58 which readily transforms to the bromo α -diketone, 59. Subsequent addition of sodium cyanide results in the isolation of 60. α -Fluoro- β -cyano epoxides (61) and α,β -dicyano epoxides (62) have been prepared similarly.⁴



Mousseron^{28,29} has observed the migration of the nitrile substituent in the rearrangement of several α -cyano epoxides. When 1-cyano-2-chlorocyclohexanol (63a) was treated with sodium ethoxide, a mixture of 1-cyanocyclohexene oxide (64a) and 2-cyanocyclohexanone (65a) was obtained. When the

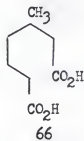


a, R=H
b, R=CH₃

reaction was carried out at 0°, the main product was the α -cyano epoxide, 64a, while at 80° the reaction gave chiefly the α -cyano ketone, 65a. α -Cyano ketone, 65a, was also obtained when the cyano epoxide, 64a, was treated with sodium ethoxide at 80°.

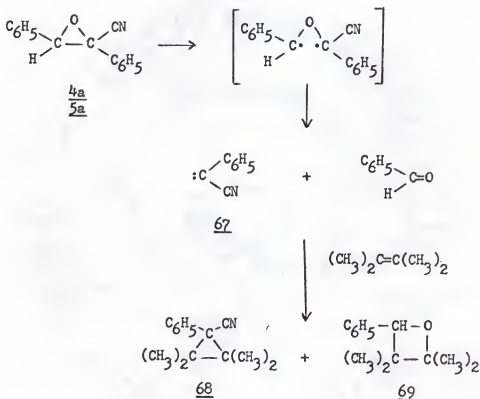
To prove the α -cyano ketone obtained was the product of cyanide migration rather than hydrogen, the reaction was performed with 1-cyano-2-chloro-5-methylcyclohexanol (63b). The product of the reaction 2-cyano-5-methylcyclohexanone (65b) was then hydrolyzed to give 3-methylpimelic acid (66).

65b



Stepanov⁴⁸ and Griffen³⁷ have independently studied the photofragmentation of α -cyano epoxides. Stepanov⁴⁸ studied the photofragmentation of a mixture of cis and trans-2,3-diphenyl-2,3-epoxypropionitrile (4a, 5a) in the presence of 2,3-dimethyl-2-butene. Benzaldehyde, 1,1,2,2-tetramethyl-3-phenyl-3-cyanocyclopropane (68), and 1,1,2,2-tetramethyl-3-phenylpropene oxide (69) were obtained. The same products were obtained in the photolysis of cyano epoxide 5a as observed by Griffen.³⁷ Photolysis for short periods of

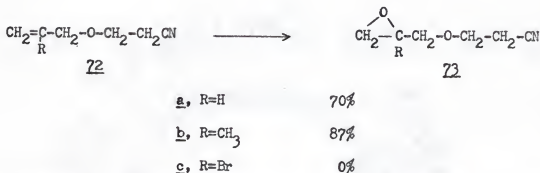
time resulted in trans to cis isomerization. Stepanov had reported that the photolysis of α -cyano epoxides, as well as other epoxides, results in the homolytic cleavage of the carbon-carbon bond (see ref. 49 and the references therein).



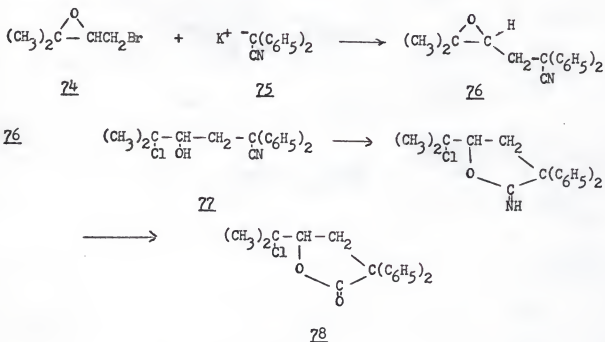
In addition, Griffen³⁷ studied the photofragmentation of 2,3,3-triphenyl-2,3-epoxypropionitrile (70) and 2-phenyl-1-oxaspiro[2.5]octane-2-carbonitrile (71) which also fragmented to give phenylcyanocarbene (67).



3-(2,3-Epoxypropoxy)propionitrile (73a) was prepared by the epoxidation of 3-(allyloxy)propionitrile (72a) with peracetic acid in chloroform.⁵² The yields of epoxide 73 increased as the electron availability of the double bond increased.



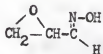
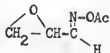
The reaction of 1-bromo-2,3-epoxy-3-methylbutane (74) with the potassium derivative of diphenylacetonitrile (75) gave 4,5-epoxy-5-methyl-2,2-diphenylhexanonitrile (76).⁵⁴ Hydrolysis of 76 with hydrochloric acid resulted in the formation of γ -lactone 78 believed to occur by the addition of hydrogen chloride to the epoxide ring giving 77, cyclization, and hydrolysis of the imino group to give 78.



α -Cyano epoxides have also been prepared, with little synthetic utility by the addition of hypochlorous acid to an α,β -unsaturated nitrile followed by treatment with base to give the epoxy nitrile.¹⁵



Finally, if epoxyalkyl aldoximes, 79, are allowed to react with a slight excess of acetic anhydride, the resulting oxime ester, 80, may be pyrolyzed in vacuo to give glycidonitrile 14a.³⁵

798014a

OBJECTIVES OF THIS INVESTIGATION

The objectives of this investigation were to synthesize and study the boron-trifluoride etherate catalyzed and thermal rearrangements of trans-2,3-diphenyl-2,3-epoxypropionitrile, trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile, and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile.

DISCUSSION OF EXPERIMENTAL RESULTS

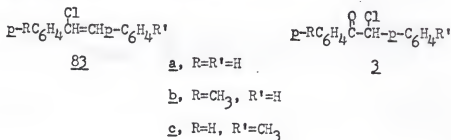
Tabor⁵³ had previously studied the catalyzed rearrangements of 1-chloro-4-methylcyclohexene oxide (81) and found that the major product was that of chlorine migration, 2-chloro-4-methylcyclohexanone (82). A similar system,



1-cyano-5-methylcyclohexene oxide (64b), was investigated by Mousseron^{28,29} who found the cyano substituent also migrated to form 2-cyano-5-methyl cyclohexanone (65b) when catalyzed with sodium ethoxide.

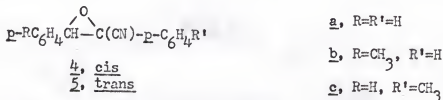


McDonald and Schwab^{24,25} studied the peracid oxidations of trans-1-chloro-1-*p*-tolyl-2-phenylethylene (83b) and trans-1-chloro-1-phenyl-2-*p*-tolylethylene (83c) which resulted in the chlorine migration of the intermediate epoxide to give *p*-methyl- α -chloro- α -phenylacetophenone (3b) and α -chloro- α -*p*-tolylacetophenone (3c), respectively.

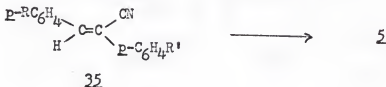


Since chlorine migration was observed in the facile rearrangement of the epoxide of 83, and cyano migration had been observed previously with 1-cyano-

5-methylcyclohexene oxide (64b), the effect of an α -cyano substituent would be of interest in the study of the epoxide-carbonyl rearrangement of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b) and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile (5c).



The syntheses of cis- (4a) and trans-2,3-diphenyl-2,3-epoxypropionitrile (5a) have been previously described in the literature, a modification of which would be used for the syntheses of 5b and 5c. Kohler and Brown²³ prepared 4a and 5a in low yields by the treatment of α -chlorodeoxybenzoin (3a) with sodium cyanide in alcohol. The synthesis described by Payne and Williams³⁶ involved the basic peroxidation of trans- α,β -diphenylacrylonitrile (35a) with tert-butylhydroperoxide in the presence of benzyltrimethylammonium hydroxide (Triton B). The latter method was chosen since only the trans isomer was obtained in good yield.



- a, R=R'=H
b, R=CH₃, R'=H
c, R=H, R'=CH₃

The syntheses of the α -cyano epoxides, 5b and 5c, were initiated by the preparation of trans- α -phenyl- β -p-tolylacrylonitrile (35b) and trans- β -phenyl- α -p-tolylacrylonitrile (35c). These α,β -diarylacrylonitriles were prepared by

the condensation of phenylacetonitrile (85b) with *p*-tolualdehyde (84b), and *p*-tolylacetonitrile (85c) with benzaldehyde (84c), respectively, in the presence of sodium ethoxide.^{3,19,57} The *trans* configuration was assigned to 35b and 35c based on the observed ultraviolet spectra of *cis*- and *trans*- α , β -diphenylacrylonitrile previously recorded.¹¹

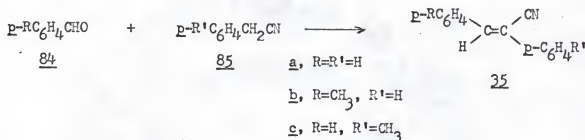


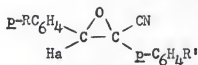
TABLE 1

OBSERVED ULTRAVIOLET SPECTRA
OF *CIS*- AND *TRANS*- α , β -DIARYLACRYLONITRILES

	λ_{max} (log ϵ)		λ_{max} (log ϵ)	
	<u>34, cis</u>		<u>35, trans</u>	
<u>a</u> ¹¹	224 (4.36)	295 (4.22)	227 (4.27)	312 (4.41)
<u>b</u>			232 (4.13)	317 (4.40)
<u>c</u>			229 (4.21)	317 (4.39)

trans-2-Phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b) and *trans*-3-phenyl-2-*p*-tolyl-2,3-epoxypropionitrile (5c) were synthesized by the method described by Payne and Williams.³⁶ The *tert*-butylhydroperoxide oxidation of 35b and 35c in the presence of benzyltrimethylammonium hydroxide resulted in the formation of 5b and 5c in 84% and 76% yields, respectively. *trans*-2,3-Diphenyl-2,3-epoxypropionitrile (5a) was also prepared for the comparison of spectral data with 5b and 5c, as shown in Table 2. The infrared and nuclear magnetic resonance (nmr) spectra are shown on pages 48 and 58.

35



5

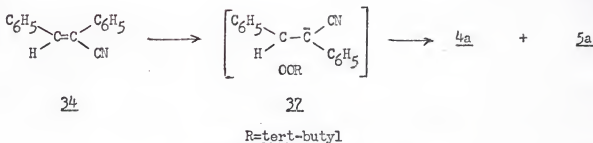
a, R=R'=Hb, R=CH₃, R'=Hc, R=H, R'=CH₃

TABLE 2

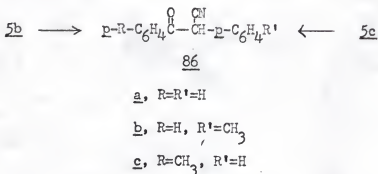
COMPARISON OF THE INFRARED AND NMR SPECTRA
OF TRANS-2,3-DIPHENYL-, TRANS-2-PHENYL-3-P-TOLYL-,
AND TRANS-3-PHENYL-2-P-TOLYL-2,3-EPOXYPROPIONITRILE.

	$\nu(\text{CN})$	$\nu(\text{sym})$	$\nu(\text{asym})$	$\tau(\text{Ha})$
<u>5</u>				
<u>a</u>	4.47	7.87	11.30	5.98
<u>b</u>	4.47	7.88	11.35	6.05
<u>c</u>	4.40	7.90	11.45	6.02

The trans configurations of the a-cyano epoxides were certain when the melting point of trans-2,3-diphenyl-2,3-epoxypropionitrile (70.0-70.5°) was compared to the melting points of the cis (79-80°)⁴⁸ and trans (67-70°)⁴⁸ isomers. Also, Zimmerman⁵⁸ has shown that the basic epoxidation of acrylonitriles occurs by the attack of the peroxide anion at the β -carbon atom (32), thus cis to trans isomerization could occur to the most stable configuration before closure of the epoxide ring. Payne³⁶ has demonstrated this fact by the epoxidation of cis- α,β -diphenylacrylonitrile (34a) with tert-butylhydroperoxide in the presence of Triton B. A complete reaction was observed, but a mixture of products was obtained; however, the trans isomer, 5a, was obtained in good yield (70%) when 35a was epoxidized under the same conditions.

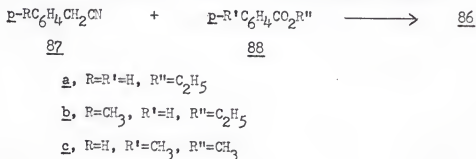


The first products considered from the rearrangements of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b) and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile (5c) were α-cyano-4-methyldeoxybenzoin (86b), the product of cyanide and hydrogen migration, respectively, and α-cyano-4'-methyldeoxybenzoin (86c), the product of hydrogen and cyanide migration, respectively.



α-Cyanodeoxybenzoin (86a) had been previously prepared by the condensation of phenylacetoneitrile (87a) with ethyl benzoate (88a) in the presence of sodium amide in ether²² and hydrogen over potassium metal in benzene.⁵⁶

α-Cyano ketone 86a was prepared in ether with sodium hydride. α-Cyano-4-methyldeoxybenzoin (86b) and α-cyano-4'-methyldeoxybenzoin (86c) were prepared similarly by the condensation of p-tolylacetoneitrile (85b) with ethyl benzoate



(87b) and phenylacetonitrile (87c) with methyl p-toluate (88c), respectively.

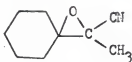
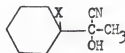
The infrared and nmr spectra of 86a, 86b, and 86c, shown on pages 54 and 64, and the carbon and hydrogen analysis were in accord with their assigned structures. Table 3 compares the nitrile and carbonyl stretching frequencies observed in the infrared spectra of 86a, 86b, and 86c, the methyne proton (Ha) observed in the nmr spectra, and their absorption maxima observed in the ultraviolet spectra.

TABLE 3

COMPARISON OF THE INFRARED, NMR, AND
ULTRAVIOLET SPECTRA OF α -CYANODEOXYBENZONES.

	$\nu(\text{CN})$	$\nu(\text{CO})$	$\tau(\text{Ha})$	$\lambda_{\text{max}} (\log \epsilon)$
<u>86</u>				
<u>a</u>	4.47	5.95	4.33	288 (4.04) 250 (3.90)
<u>b</u>	4.48	5.95	4.37	293 (4.14)
<u>c</u>	4.45	5.97	4.37	290 (4.12)

The borontrifluoride etherate catalyzed rearrangements of the α -cyano epoxides, 5a, 5b, and 5c, were chosen since the rearrangement of α -cyano epoxides with catalytic amounts of borontrifluoride etherate had never been investigated and cyanide migration might be observed in the epoxide-carbonyl rearrangement. The rearrangements of α -cyano epoxides with mineral acids

2021 X=Cl24 X=F

(HCl, HF),⁵⁰ and mineral acids in the presence of Lewis acids (ZnCl₂, HCl; BF₃, HF)^{5,50} resulted in the formation of the respective α -halo cyanohydrin (21, 24). Excess borontrifluoride etherate catalyzed rearrangements also resulted in the formation of α -fluoro cyanohydrin 24.⁵⁰

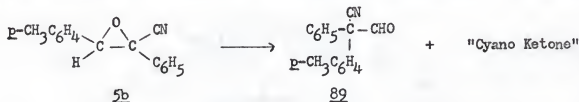
The borontrifluoride etherate rearrangements of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b) and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile (5c) were first attempted in ether, but little or no rearrangement of the epoxide was observed. If the rearrangement of the α -cyano epoxides, 5b and 5c, were carried out in benzene, complete rearrangement was observed almost immediately. The ratio of products formed was also found to be independent of the concentration of borontrifluoride etherate used in the rearrangement.

The rearrangement of 5b resulted in the formation of two products as observed by spectroscopy. The nmr spectrum of the mixture of products obtained exhibited peaks at τ 0.53 and τ 4.88 in a ratio 0.89. Other peaks observed were those for the aromatic (τ 2.70-2.95) and methyl hydrogens (τ 7.71). Addition of deuterium oxide to the nmr sample resulted in no exchange with deuterium, indicating no acidic proton was present. The infrared spectrum exhibited two nitrile absorptions at 4.50 (μ) and 4.55 (μ), but only one carbonyl stretching frequency at 5.85 (μ) (s).

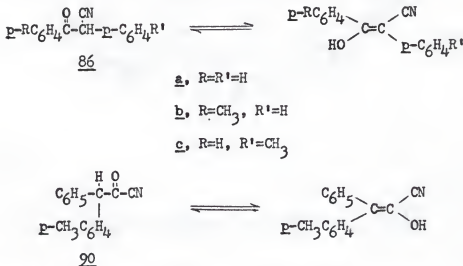
If the benzene solution was treated with a saturated solution of sodium bicarbonate in the work-up procedure, the peak at τ 4.88 observed in the nmr spectrum was absent. Addition of deuterium oxide to this sample also resulted in no noticeable exchange with deuterium; however, the infrared spectrum exhibited a strong OH absorption at 3.14 (μ) in addition to those previously observed.

The above spectral data suggested that the products obtained from the

borontrifluoride etherate rearrangement of 5b was an aldehyde (47%) and a cyano ketone (53%), which was easily enolized in the presence of base. The structure of the aldehyde was tentatively assigned to g-cyanophenyl-p-tolyl-acetaldehyde (89), the product obtained from p-tolyl migration. No tentative

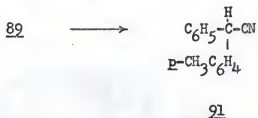


assignment could be made for the structure of the cyano ketone since the g-cyanodeoxybenzoins are reported to readily undergo keto-enol tautomerization.³⁹ However, the spectral data of 86b and 86c do not agree with the spectra observed for either rearrangement product from 5b. This cyano ketone product was then considered to possibly be phenyl-p-tolylpyruvonnitrile (90), the product of phenyl migration, which enolized when treated with mild base.



The separation of 89 and the cyano ketone was very difficult since both were very reactive in the presence of base. Separation of the products by column chromatography was difficult with silica gel since both 89 and the cyano ketone eluted at approximately the same rate. The attempted separation

of 89 and cyano ketone on neutral alumina gave only phenyl-*p*-tolylacetonitrile (91), the apparent product from decarbonylation of the aldehyde, 89.

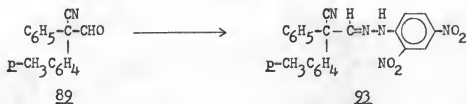


The infrared and nmr spectra (pages 50 and 60) are in accord with the structure of phenyl-*p*-tolylacetonitrile (91). The nmr spectrum exhibited a peak at τ 5.03 for the methyne hydrogen (Ha) along with those observed for the aromatic (τ 2.77, 2.90) and methyl (τ 7.70) hydrogens. The infrared spectrum exhibited nitrile absorption 4.50μ . The melting point was identical to that previously recorded for phenyl-*p*-tolylacetonitrile.²⁷ Molecular weight determination in chloroform gave a molecular weight of 207. The structure of nitrile 91 was verified by hydrolysis in 70% sulfuric acid. The infrared and nmr spectra, and the melting point were in accord with the structure of phenyl-*p*-tolylacetamide (92).

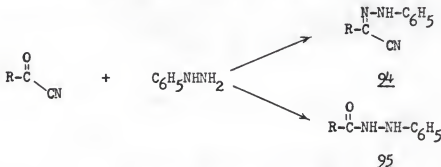


Since the separation of α -cyanophenyl-*p*-tolylacetaldehyde (89) and the cyano ketone by column chromatography had failed, the preparation of the 2,4-dinitrophenylhydrazones and subsequent separation of the two derivatives by fractional recrystallization was attempted. When the mixture of 89 and the cyano ketone was treated with a slight excess of 2,4-dinitrophenylhydrazine reagent, only 2,4-dinitrophenylhydrazine reagent was obtained along with the 2,4-dinitrophenylhydrazone derivative of the aldehyde, 89. If a slight excess

of the reagent was used over the amount of aldehyde present from the rearrangement of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b), the 2,4-dinitrophenylhydrazone 93 was obtained in 41% yield. No other 2,4-dinitrophenylhydrazone derivative could be isolated. The infrared and nmr spectra of 93 were in accord with the assigned structure.



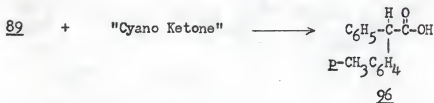
If the cyano ketone was present, the formation of a 2,4-dinitrophenylhydrazone derivative would have been anticipated; however, α -ketonitriles (acyl cyanides) have been shown to react with phenylhydrazine to give two products, resulting from the displacement of cyanide (94) as well as formation of the phenylhydrazone derivative 94.⁵⁵ If the 2,4-dinitrophenylhydrazine analog of 95 was formed, this would explain why no 2,4-dinitrophenylhydrazine derivative was obtained for 90; however, this was not observed.



Since the isolation of this unknown compound previously believed to be a cyano ketone had failed by previous methods, and since the structure of the aldehyde had been established, extraction of an aqueous potassium carbonate-ethanol solution of 89 and the unknown with ether was tried. On acidification of the basic solution, phenyl-p-tolylacetic acid (96) was obtained, rather

than the unknown.

The infrared and nmr spectra, recorded on pages 50 and 60, gave conclusive evidence that the product obtained was 96. The infrared spectrum exhibited an OH absorption at 3.40μ and a carbonyl absorption at 5.90μ . No absorption was observed for a nitrile substituent. The nmr spectrum exhibited a peak at τ 5.01 for the methyne proton (Ha) in addition to those observed for the aromatic hydrogen (τ 2.74 and 2.97) and acid (τ -1.85) protons. The nmr spectrum of the additional products obtained indicated a mixture of phenyl-p-tolylacetonitrile (91) and a compound which exhibited a similar spectrum, but which had never been isolated before. This product was not further investigated.



Base extraction of the mixture in ether was again tried with a dilute aqueous solution of potassium carbonate. Upon rapid separation and acidification, the aqueous solution gave an alcohol, believed to be the enol of the cyano ketone, 86b, 86c, or 90. A mixture of o-cyano phenyl-p-tolylacetaldehyde (89) and phenyl-p-tolylacetonitrile (91) was also obtained from the original ether layer which was completely converted to 91 when chromatographed on neutral alumina.

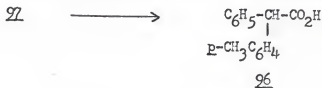
The nmr spectrum (page 62) of the enol exhibited a broad absorption (OH) centered at τ 4.05 which disappeared on addition of deuterium oxide. Other than the peaks observed for the aromatic hydrogens, two peaks were observed at τ 7.67 and τ 7.69 for the methyl hydrogens. The methyl peaks observed were initially explained as keto-enol tautomerization of the cyano ketone, 86b,

86c, or 90, since a polar solvent, CDCl_3 , was used to dissolve the sample. Russell³⁹ had shown that the keto-enol tautomerism of α -cyanodeoxybenzoin (86a) did occur even in nonpolar solvents. The infrared spectrum (KBr, page 52) exhibited OH absorption at 3.09μ and nitrile absorption at 4.50μ . No absorption band for a carbonyl was observed. The infrared spectrum exhibited similar absorptions in chloroform (15%, page 52). The fact that two different methyl absorptions were observed in the nmr spectrum indicated that two different isomers of the enol were being observed, rather than keto-enol tautomerism. A tentative assignment of the structure of the enol is α -hydroxy- β -phenyl- β -p-tolylacrylonitrile (97).



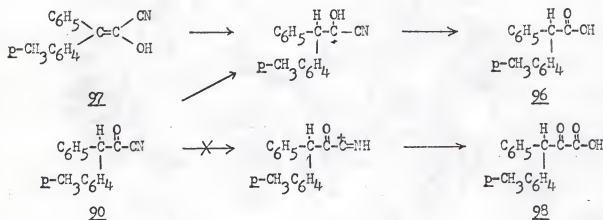
The ultraviolet spectrum of 97 (page 68) was similar to the spectra observed for the α -cyanodeoxybenzoins, 86a, 86b, and 86c, (Table 3), but exhibited a greater molar absorptivity. These spectral data also indicate that this product is not α -cyano-4-methyldeoxybenzoin (86b) or α -cyano-4'-methyldeoxybenzoin (86c).

Further evidence was obtained for the structure of enol 97 by the hydrolysis with 25% aqueous sulfuric acid and 5% aqueous sodium hydroxide at 100° . In each case, phenyl-p-tolylacetic acid (96) was obtained. Acid 96 was also obtained from the basic hydrolysis of the mixture of the borontrifluoride etherate rearranged products of trans-2-phenyl-3-p-tolyl-2,3-epoxypropioni-

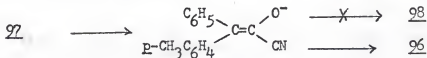


trile (5b) in ethanol.

The acid hydrolysis of acylcyanides (α -ketonitriles) has been shown to produce the respective acid under either strong or weak acid conditions.^{18,55} The same result would be anticipated with the hydrolysis of enol 97. Protonation of the carbonyl of the keto form or the β -carbon atom of the enol form followed by attack with water and elimination of cyanide ion would give the diarylacetic acid, 96. Protonation of the nitrile group would be expected to result in the formation of phenyl-p-tolylpyruvic acid 98, which was not observed.



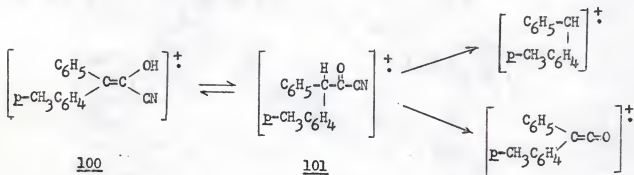
The hydrolysis of enol 97 in base under ideal conditions was anticipated to give 98; however, the hydrolysis with aqueous potassium carbonate in ethanol at room temperature and aqueous sodium hydroxide at 100° gave 96.



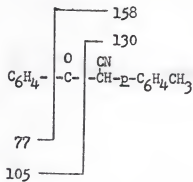
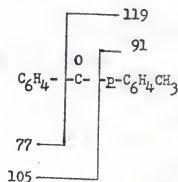
To verify that α -cyano-4-methyldeoxybenzoin (86b) was not formed from the borontrifluoride rearrangement of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b), 86b was hydrolyzed under identical conditions with 25% aqueous sulfuric acid. Essentially no hydrolysis was observed, but under more vigorous conditions, 4-methyldeoxybenzoin (99) was obtained as anticipated.



Conclusive evidence was obtained for the structure of α -hydroxy- β -phenyl- β -p-tolylacrylonitrile (97) from the mass spectrum of this compound (page 66) when compared to the mass spectrum of α -cyano-4-methyldeoxybenzoin (86b) (page 66). The shift from the enol form 100, to the α -ketonitrile form, 101, was observed by the loss of 27 m/e (HCN) and 54 m/e (COCN) from the parent ion (235 m/e) in the mass spectrum of 97.



Other peaks observed at 196, 165, 119, and 105 m/e could not be explained by the fragmentation of the α -ketonitrile, 101, or the fragmentation of α -cyano-4-methyldeoxybenzoin (86b). However, oxidation of 97 could occur within the mass spectrometer at 70 ev to give 4-methylbenzophenone (102),

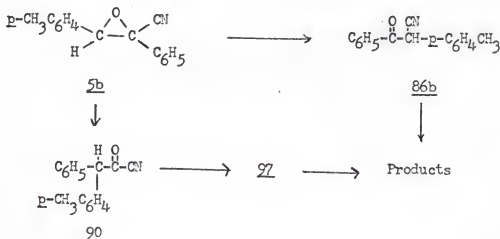
86b102

which would explain the observed peaks at 196, 119, and 105 m/e. These peaks were found to decrease in intensity in subsequent spectra, and completely disappeared when observed at 11 ev. The origin of the peak observed at 165 m/e is uncertain.

The methyl vinyl ether of enol 97 was prepared by its reaction with excess diazomethane. The infrared and nmr spectra (pages 52 and 62) and the carbon and hydrogen analysis were in accord with the structure of α -methoxy- β -phenyl- β -p-tolylacrylonitrile (103).



α -Cyano-4-methyldeoxybenzoin (86b) and 97 were individually treated with borontrifluoride etherate as employed for the rearrangement of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b). In each case no further rearrangement was observed. The possibility of forming 86b, the product of cyanide migration in the rearrangement of the epoxide, was therefore eliminated since further rearrangement did not occur to give the observed products. The fact that 97 also did not rearrange under the same conditions indicated that the products observed are those directly obtained from the rearrangement.



The rearrangement of 5b, as observed by nmr spectroscopy in benzene, also indicated the products formed were those obtained directly from the rearrangement. The products obtained were formed immediately on addition of borontrifluoride etherate. Addition of excess borontrifluoride etherate did not alter the distribution of products.

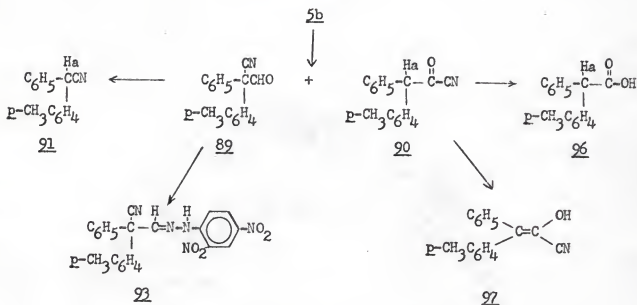
The correlation of the methyne hydrogen (H_a) observed in the nmr spectra of diarylacetic acid and its derivatives with the rearranged products observed (Table 4), and the reactions performed on the rearranged products, as shown in Scheme 1, gave conclusive evidence that the products obtained from the borontrifluoride etherate catalyzed rearrangement of trans-2-phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b) are α -cyanophenyl-*p*-tolylacetaldehyde (89) and phenyl-*p*-tolylpyruvonnitrile (90), the products of *p*-tolyl and phenyl migration, respectively.

TABLE 4

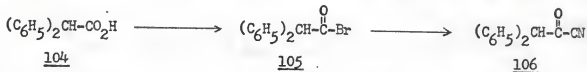
COMPARISON OF NMR SPECTRA OF
PHENYL-*p*-TOLYLACETIC ACID AND ITS DERIVATIVES
WITH PHENYL-*p*-TOLYLPYRUVONITRILE.

	τ_{H_a}
Phenyl- <i>p</i> -tolylacetoneitrile (<u>91</u>)	5.05
Diphenylacetic Acid ⁴³	5.04
Phenyl- <i>p</i> -tolylacetic Acid (<u>96</u>)	5.03
Phenyl- <i>p</i> -tolylacetamide (<u>92</u>)	5.13
Phenyl- <i>p</i> -tolylpyruvonnitrile (<u>90</u>)	4.88

SCHEME 1



To prove that phenyl-*p*-tolylpyruvonnitrile (90) was a product in the rearrangement of 5b, the synthesis of diphenylpyruvonnitrile (106) was attempted. Diphenylacetic acid (104) was chosen because similar physical properties would be exhibited, and only one isomer would be obtained if the enol isomer was more stable than the ketone isomer. The procedure described by Oakwood and Weisgerber³² for the reaction of acid chlorides with cuprous cyanide was tried with diphenylacetyl bromide, but diphenylpyruvonnitrile (106) was not formed. Schrieber's⁴⁶ method for the reaction of acid halides with cuprous cyanide in benzene at 100° was also tried with 105. 106 was obtained in low yield.



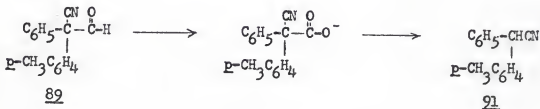
The borontrifluoride etherate catalyzed rearrangement of *trans*-3-phenyl-2-*p*-tolyl-2,3-epoxypropionitrile (5c) resulted in the formation of a single product. Similar infrared and nmr spectra were obtained for this product as obtained for the aldehyde from the borontrifluoride etherate catalyzed

rearrangement of trans-2-phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b). The nmr spectrum exhibited a peak at τ 0.48 for the aldehyde proton along with those for the aromatic hydrogens (τ 2.68 and 2.87) and the methyl hydrogens (τ 7.67). The infrared spectrum exhibited an absorption at 4.45μ for the nitrile and 5.75μ for the carbonyl.

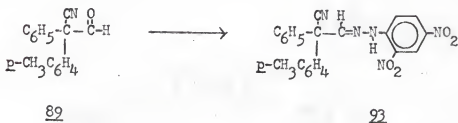
Attempted purification by column chromatography on neutral alumina also resulted in conversion of the aldehyde to phenyl-*p*-tolylacetonitrile (91) in 91% yield. The infrared and nmr spectra, and the melting point were in agreement to those previously obtained for 91 from the chromatography of the rearranged products of trans-2-phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b). Distillation and bisulfite addition of the aldehyde also resulted in quantitative yields of phenyl-*p*-tolylacetonitrile; however, if a benzene solution of the aldehyde, 89, is treated briefly with a dilute solution of sodium bicarbonate, 89 is obtained in a fairly pure state.



The presence of the aldehyde was confirmed by precipitation of silver obtained when 89 was treated with Tollen's reagent. Nitrile 91 was obtained after acidification. The infrared and nmr spectra, and the melting point were in agreement with those obtained for 91 from the chromatography of the α -cyano epoxides 5b and 5c.

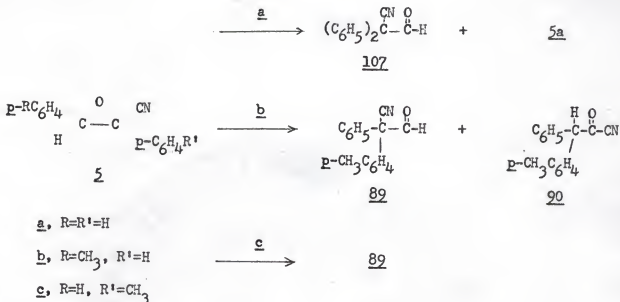


The 2,4-dinitrophenylhydrazone of 89 gave identical infrared and nmr spectra, and melting point to those previously obtained for this compound.

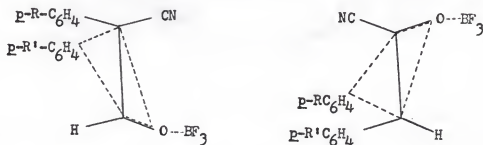


Since phenyl and *p*-tolyl migration are found in the borontrifluoride catalyzed rearrangement of 5b and only phenyl migration is observed from similar treatment of 5c, the rearrangement of trans-2,3-diphenyl-2,3-epoxypropionitrile (5a) was done under identical conditions to compare the ratios of products observed. The nmr spectrum of the rearranged products obtained indicated incomplete rearrangement of 5a and exhibited a major peak at τ 2.64 (aromatic hydrogens) and a peak at τ 5.94 equivalent to 0.63 hydrogens, which were identical to those in the nmr spectrum observed for 5a. An additional peak was observed at τ 0.45 equivalent to 0.37 hydrogens. The infrared spectrum exhibited a carbonyl absorption at 5.77μ in addition to the nitrile absorption at 4.45μ . Comparison of the spectra of the products obtained from the rearrangement of 5a with the spectra for 89 indicated that 37% of α -cyano-diphenylacetaldehyde (107) was obtained.

The borontrifluoride etherate catalyzed rearrangements of trans-2,3-diphenyl-2,3-epoxypropionitrile (5a), trans-2-phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b), and trans-3-phenyl-2-*p*-tolyl-2,3-epoxypropionitrile (5c) resulted in phenyl and *p*-tolyl migration rather than cyanide migration.

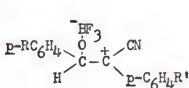


If the rearrangement occurred by a concerted mechanism, the stereochemistry of the transition state would be nearly the same for 5a, 5b, and 5c. If we assume little or no charge build up, then rearrangement of the best migrating group should be the major control on product formation and similar products should be observed from 5a, 5b, and 5c. Stereochemistry is not a controlling factor since all are trans.³³ If the rearrangement could occur by



a two stage process involving a rate determining unimolecular cleavage of the epoxide ring of the complexed α -cyano epoxides, 108, the most stable carbonium ion would be formed followed by the fast migration of the best leaving group. Since the effect of an electron releasing group would be most strongly felt by the two step process, we conclude that it most probably is the mechanism in

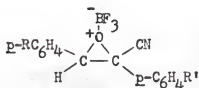
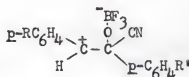
operation for these catalyzed rearrangements of the trans-diaryl- α -cyano epoxides.

110

37%

47%

100%

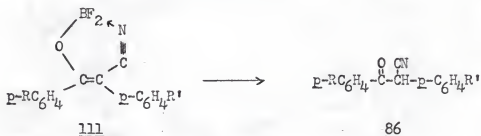
108a, R=R'=Hb, R=CH₃, R'=Hc, R=H, R'=CH₃109

53%

For the case of the rearrangement of 5a, only α -cyanodiphenylacetaldehyde (107) was obtained in high yield, although in only 37% conversion, arising apparently only from 110a. The rearrangement of 5b results in the formation of α -cyanophenyl-*p*-tolylacetaldehyde (89; 47%) and phenyl-*p*-tolylpyruvonitrile (90; 53%), which indicates that the stability of the α -cyanobenzyl cation, 110b, is nearly equal to the stability of the *p*-methylbenzyl cation, 109b. Only the aldehyde, 89, was formed from the rearrangement of 5c which indicated the added stability of 110c due to the electron releasing *para* methyl group to give predominately aldehyde, 89. Such an overriding influence by a *p*-methyl group is not expected and makes these arguments somewhat suspect.

Since the rearrangements of the α -cyano epoxides, 5a, 5b, and 5c were performed with borontrifluoride etherate, the molecule which rearranged was the complex. The role of the borontrifluoride molecule in the formation of complexes with ether in the presence of a nitrile substituent is not clearly understood. Stable borontrifluoride complexes with the nitrogen of the nitrile substituent have been observed in the presence of methoxy ethers and

nitro groups.¹⁷ If this was observed, no rearrangement would occur until the concentration of borontrifluoride etherate was greater than the concentration of the epoxide present. Since the concentration dependency was not observed, one molecule of borontrifluoride could complex with either the oxygen or the nitrogen of the nitrile by the loss of HF to give the complex 111; however, on hydrolysis the product obtained would be that of hydrogen migration rather than phenyl and *p*-tolyl migration, which was observed.



The borontrifluoride complex formed in benzene could equilibrate between the nitrogen of the nitrile and the epoxide oxygen, depending on the relative basicities of these two atoms, to lead eventually to the products observed.



The nitrile substituent does obviously alter the course of the rearrangements of the *trans*-diaryl- α -cyano epoxides, 5a, 5b, and 5c, compared to the analogous α -chloro epoxides in which the major process involves chloride migration with borontrifluoride.

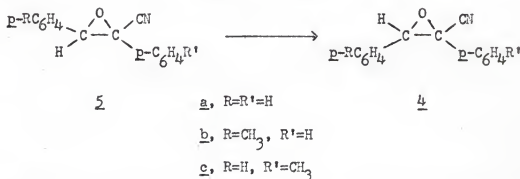
Since the borontrifluoride etherate catalyzed rearrangements of the α -cyano epoxides, 5a, 5b, and 5c, did not rearrange to products through the migration of the cyanide substituent, the thermal rearrangements were also considered. The thermal rearrangements of α -cyano epoxides had never been

investigated; however, chloride migration had been observed by Tabor⁵³ in the thermal rearrangement of 1-chloro-4-methylcyclohexene oxide (81).



trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b) and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile (5c) were individually and successively passed through a column heated to 360°. The ratio of rearranged products to epoxide was observed by nmr spectroscopy.

A sample of product from thermally rearranged 5b was obtained by column chromatography on neutral alumina. The infrared and nmr spectra of this product gave conclusive evidence that trans to cis isomerization (from 5b to 4b) had occurred. The infrared spectrum exhibited absorptions at 4.45 μ for the nitrile and at 8.48 and 11.16 μ which were assigned to the symmetric and asymmetric stretch of the epoxide ring.^{2,31} The nmr spectrum of 4b exhibited peaks at τ 2.70, 3.10, 5.32, and 7.77 which were different than those observed for the trans isomer.



The trans to cis isomerization of 5b and 5c could be explained by either cleavage of the carbon-carbon bond or carbon-oxygen bond of the epoxide ring.

Isomerization from trans to cis has also been observed by cleavage of the carbon-carbon bond when trans-2,3-diphenyl-2,3-epoxypropionitrile (5a) was photolyzed for short periods of time.⁴⁸ There is, however, insufficient evidence to conclude which mode of cleavage occurs thermally to isomerize epoxides.

SUMMARY

Few reports of α -cyano epoxides have appeared in the literature, and in most instances the compounds prepared have proven to be stable. Previous reactions have shown that α -cyano epoxides readily form α -halo cyanohydrins with mineral acids and Lewis acids. The present investigation was undertaken to prepare several α -cyano epoxides and to study their catalytic rearrangements with borontrifluoride etherate to see if cyanide migration occurs.

The basic peroxidation of trans- α,β -diphenylacrylonitrile (35a), trans- α -phenyl- β -p-tolylacrylonitrile (35b), and trans- β -phenyl- α -p-tolylacrylonitrile (35c) with basic tert-butylhydroperoxide resulted in the formation of trans-2,3-diphenyl-2,3-epoxypropionitrile (5a), trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (5b), and trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile (5c), respectively.

The borontrifluoride etherate catalyzed rearrangement of 5a gave 37% α -cyanodiphenylacetaldehyde (107) and unrearranged 5a, while the rearrangement of 5b gave 47% α -cyanophenyl-p-tolylacetaldehyde (89) and 53% phenyl-p-tolylpyruvonitrile (90). 5c gave 100% 89. Phenyl and p-tolyl migration were observed in these rearrangements; no cyanide migration was observed. The structure of 89 was proven by its spectral correlations, by its reactivity with base to give phenyl-p-tolylacetoneitrile (90) and by the isolated 2,4-dinitrophenylhydrazone derivative. The structure of 90 was proven by its spectral correlations, and by the acidic and basic hydrolyses of the enol, obtained by basic extraction of the keto form, to give phenyl-p-tolylacetic acid (96).

The rearrangements of the α -cyano epoxides to give the aldehydes 89 and 107, and the α -ketonitrile, 90, is explained in terms of the initial formation of the most stable carbonium ion prior to the migration of a phenyl or p-tolyl substituent.

The neat thermal rearrangements of 5b and 5c resulted in trans to cis isomerization.

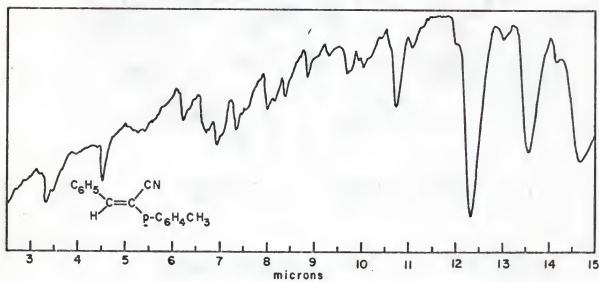
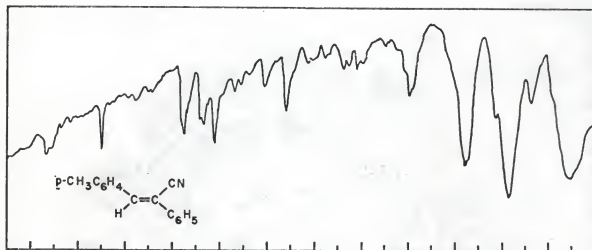
INFRARED SPECTRA

trans- α -Phenyl- β -p-tolylacrylonitrile

(KBr)

trans- β -Phenyl- α -p-tolylacrylonitrile

(KBr)



INFRARED SPECTRA

trans-2,3-Diphenyl-2,3-epoxypropionitrile

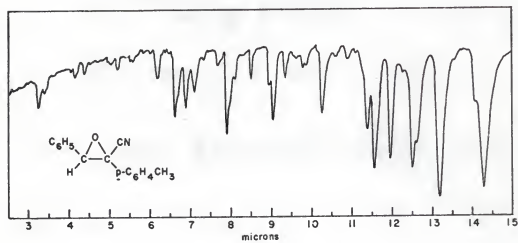
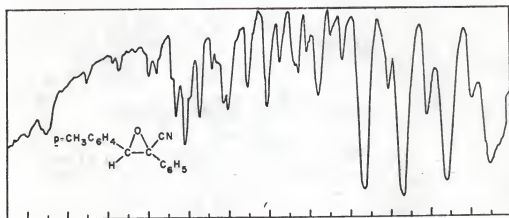
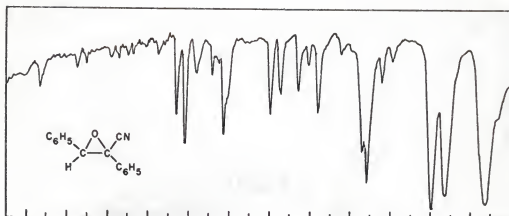
(KBr)

trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile

(KBr)

trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile

(KBr)



INFRARED SPECTRA

Phenyl-p-tolylacetonitrile

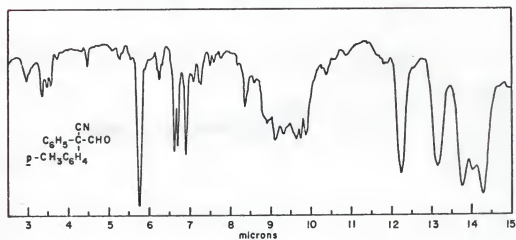
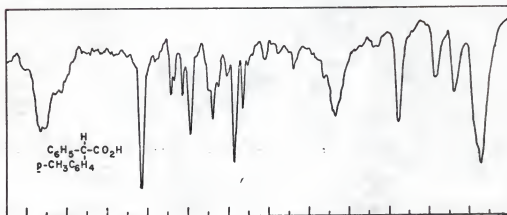
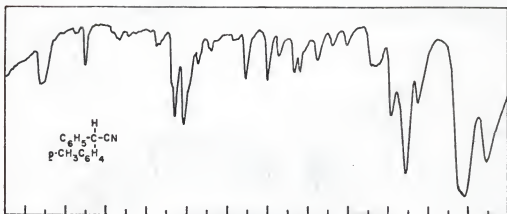
(KBr)

Phenyl-p-tolylacetic Acid

(KBr)

α -Cyanophenyl-p-tolylacetaldehyde

(Neat)

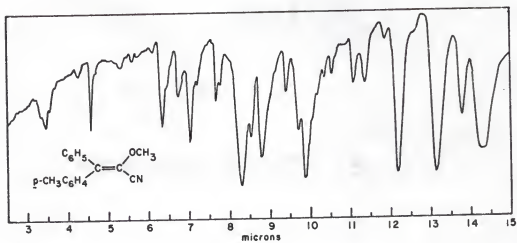
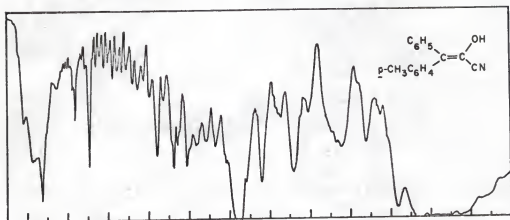
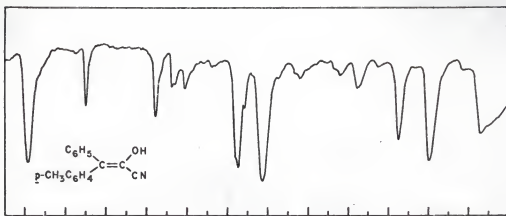


INFRARED SPECTRA

α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile
(Enol Form of Phenyl-p-tolylpyruvonitrile)
(KBr)

α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile
(Enol Form of Phenyl-p-tolylpyruvonitrile)
(15%, CHCl_3)

α -Methoxy- β -phenyl- β -p-tolylacrylonitrile
(KBr)



INFRARED SPECTRA

α -Cyanodeoxybenzoin

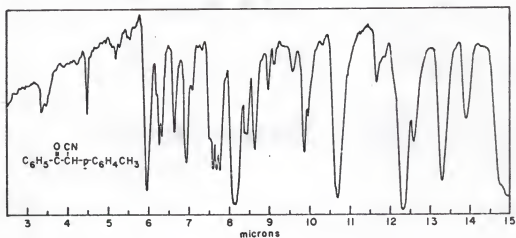
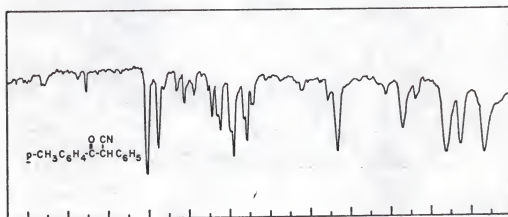
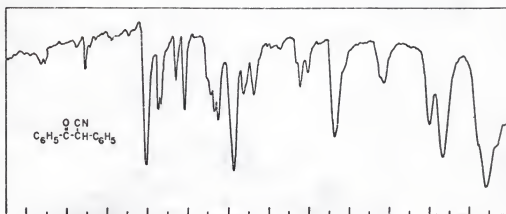
(KBr)

α -Cyano-4'-methyldeoxybenzoin

(KBr),

α -Cyano-4-methyldeoxybenzoin

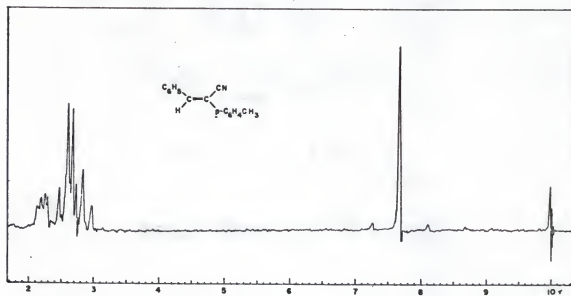
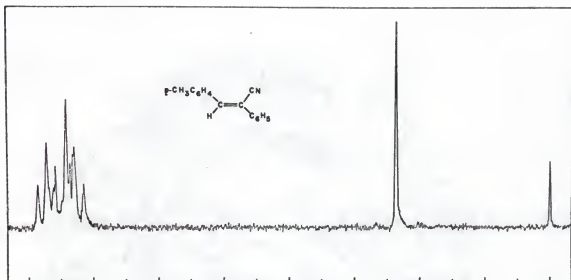
(KBr)



NMR SPECTRA

trans- α -Phenyl- β -p-tolylacrylonitrile
(in CCl_4 with TMS internal standard)

trans- β -Phenyl- α -p-tolylacrylonitrile
(in CCl_4 with TMS internal standard).



NMR SPECTRA

trans-2,3-Diphenyl-2,3-epoxypropionitrile

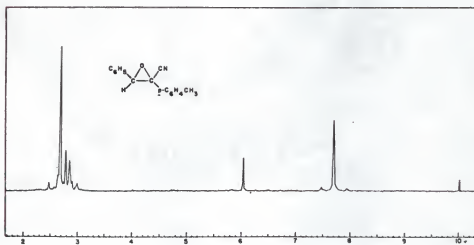
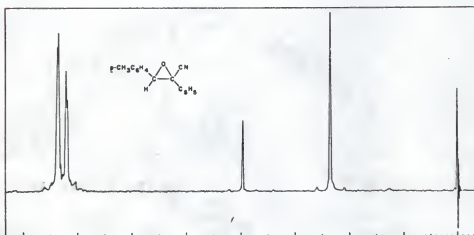
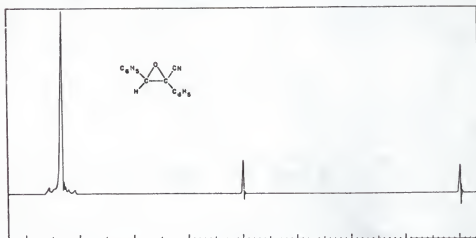
(in CCl₄ with TMS internal standard)

trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile

(in CCl₄ with TMS internal standard)

trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile

(in CCl₄ with TMS internal standard)



NMR SPECTRA

Phenyl-p-tolylacetonitrile

(in CCl_4 with TMS internal standard)

Phenyl-p-tolylacetic Acid

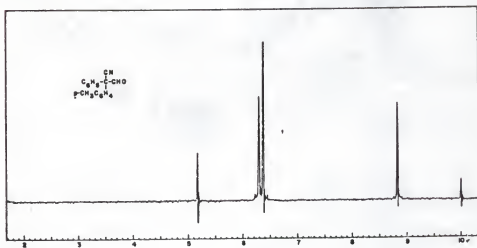
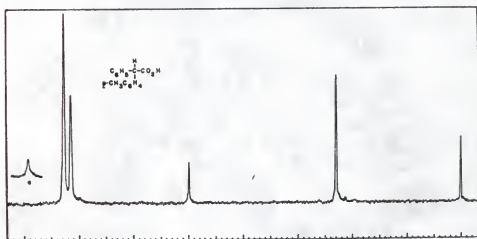
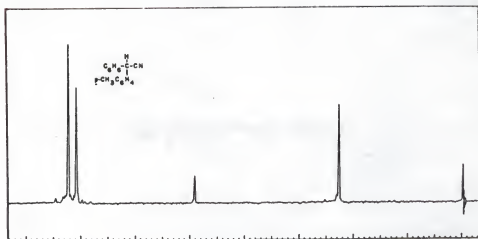
(in CDCl_3 with TMS internal standard)

a. Sweepoffset 235 cps

α -Cyanophenyl-p-tolylacetaldehyde

(in CCl_4 with TMS internal standard)

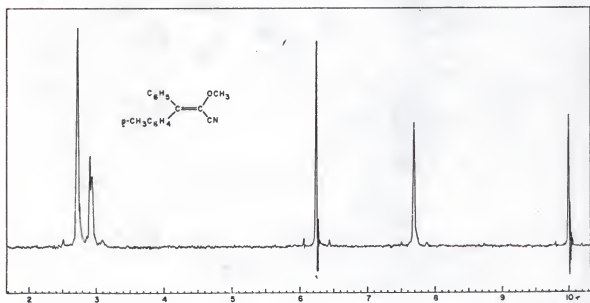
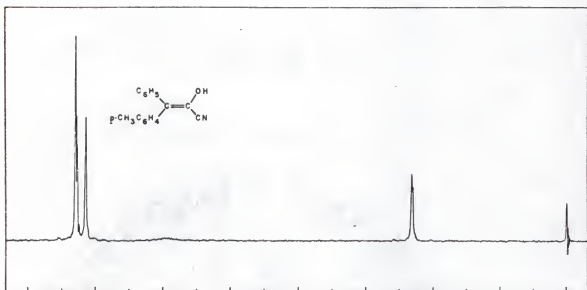
(Sweepwidth 1000 cycles)



NMR SPECTRA

α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile
(Enol Form of Phenyl-p-tolylpyruvonitrile)
(in CDCl_3 with TMS internal standard)

α -Methoxy- β -phenyl- β -p-tolylacrylonitrile
(in CCl_4 with TMS internal standard)



NMR SPECTRA

α -Cyanodeoxybenzoin

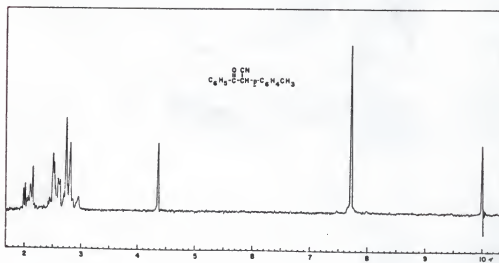
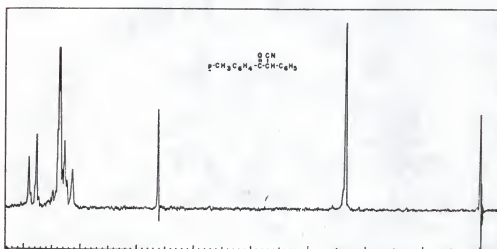
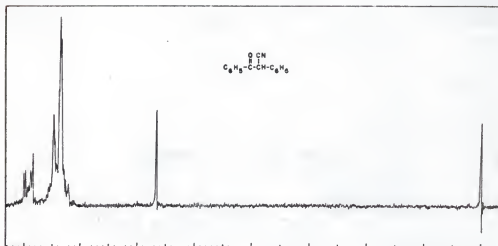
(in CDCl_3 with TMS internal standard)

α -Cyano-4'-methyldeoxybenzoin

(in CDCl_3 with TMS internal standard)

α -Cyano-4-methyldeoxybenzoin

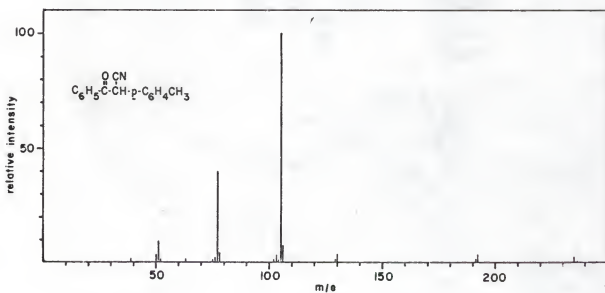
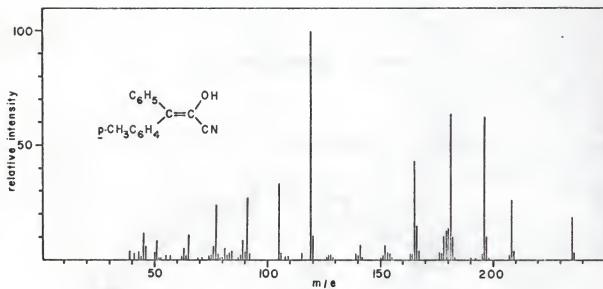
(in CDCl_3 with TMS internal standard)



MASS SPECTRA

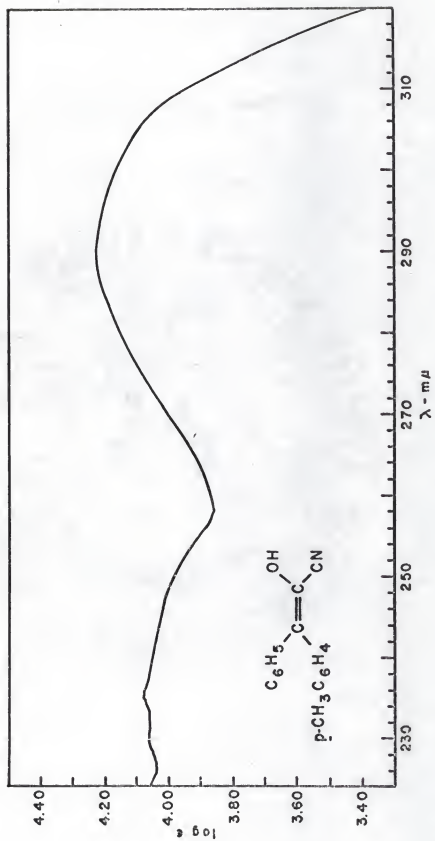
α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile
(Enol Form of Phenyl-p-tolylpyruvonitrile)
(70 ev)

α -Cyano-4-methyldeoxybenzoin
(70 ev)



ULTRAVIOLET SPECTRA

α -Hydroxy- β -phenyl- γ -p-tolylacrylonitrile
(Enol Form of Phenyl-p-tolylpyruvonitrile)
(ethanol)



EXPERIMENTAL⁶⁰

Phenylacetonitrile. A similar procedure to that previously described was used for the preparation of this compound.¹ To 60 ml of 95% ethanol was added 38.0 g (0.30 moles) of benzyl chloride followed by 20 g (0.40 moles) of sodium cyanide dissolved in 25 ml of water. The reaction mixture was heated at reflux for three and one-half hours. After cooling, the precipitated sodium chloride was filtered off, and the filtrate distilled under reduced pressure to obtain 25.6 g (73% yield) of phenylacetonitrile, b.p. 100°/8 mm (lit.¹ 115-120°/10 mm).

The infrared and nmr spectra were identical to those recorded for phenylacetonitrile.^{40,44} The infrared spectrum exhibited nitrile absorption at 4.55 μ and the nmr spectrum (CCl₄, internal TMS) exhibited absorptions at τ 2.73 (singlet, 5, aromatic) and 6.38 (singlet, 2, methylene).

p-Tolylacetonitrile. To a solution of 300 ml of chloroform containing 142.0 g (1.34 moles) of p-xylene irradiated with a modified AH-4 ultraviolet lamp, bromine was added dropwise allowing a slight excess and continued until a white precipitate had formed and the solution remained a light yellow. The chloroform solution was washed with water and distilled to remove chloroform and excess p-xylene (40.6 g).

The residue was dissolved in 225 ml of 95% ethanol and treated with 59.0 g (1.18 moles) sodium cyanide. After cooling, the precipitated sodium bromide was filtered off and the filtrate was distilled under reduced pressure. p-Tolylacetonitrile [54.4 g, 0.48 moles, b.p. 129-30°/16 mm, (lit.¹² 83°/1.5 mm)] was obtained in 55% yield based on the amount of bromine used in the reaction.

The infrared spectrum was identical to that recorded for p-tolylacetonitrile.⁴² The infrared spectrum exhibited nitrile absorption at 4.55 μ , and

the nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.90 (singlet, 4, aromatic), 6.62 (singlet, 2, methylene) and 7.68 (singlet, 3, methyl). trans- α -Phenyl- β -p-tolylacrylonitrile. The method of preparation of this compound is similar to the procedure described by Wawzonek and Smolin⁵⁷ for the preparation of trans- α , β -diphenylacrylonitrile. Fifteen ml of sodium ethoxide in ethanol (2.0 g of sodium added to 16 ml of absolute ethanol) was added dropwise to a well stirred solution of 39.7 g (0.33 moles) of p-tolualdehyde and 38.6 g (0.33 moles) of phenylacetonitrile in 200 ml of 95% ethanol. On addition of the sodium ethoxide, the solution turned dark brown and a precipitate formed. The cooled solution was filtered, and the crude product was repeatedly recrystallized from ethanol until no change in melting point occurred. α -Phenyl- β -p-tolylacrylonitrile, 37.2 g (52% yield), was obtained, m.p. 58.5-59.0° (lit.³ m.p. 61°).

A conformational assignment of trans- α -phenyl- β -p-tolylacrylonitrile can be made based on the observed ultraviolet spectrum which exhibited absorption maxima at 232 ($\log \epsilon$, 4.13) and 317 $m\mu$ ($\log \epsilon$, 4.40). The infrared spectrum exhibited nitrile absorption at 4.53 μ and the nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.10-2.90 (complex multiplet, 10, aromatic and ethene), 7.65 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 46 and 56.

trans- β -Phenyl- α -p-tolylacrylonitrile. The procedure for the preparation of this compound is the same as for trans- α -phenyl- β -p-tolylacrylonitrile. To a well stirred solution of 47.7 g (0.36 moles) of p-tolylacetonitrile and 41.7 g (0.39 moles) of benzaldehyde in 250 ml of 95% ethanol, 3.5 g of sodium ethoxide in 25 ml of ethanol was added dropwise. On addition of the sodium ethoxide, the solution turned from a cloudy white to a dense white slurry. After cooling, the reaction was filtered and the white solid obtained was

recrystallized from ethanol. β -Phenyl- α -p-tolylacrylonitrile, 69.6 g (87% yield), was obtained, m.p. 77.5-78.0° (lit.¹⁹ m.p. 74°).

The infrared spectrum exhibited nitrile absorption at 4.52μ and the nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.10-3.00 (complex multiplet, 10, aromatic and ethene) and 7.69 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 46 and 56. The ultraviolet spectrum exhibits absorption maxima at 229 ($\log \epsilon$, 4.21) and 317 $m\mu$ ($\log \epsilon$, 4.39) and allows the conformation of trans- β -phenyl- α -p-tolylacrylonitrile to be made.

trans-2,3-Diphenyl-2,3-epoxypropionitrile. The procedure for the preparation of this compound is the same as previously described by Payne and Williams.³⁶ The trans-2,3-diphenyl-2,3-epoxypropionitrile (8.7 g) was repeatedly recrystallized from methyl alcohol to obtain 5.0 g (59% yield) of product, m.p. 70.0-70.5° (lit.³⁶ m.p. 70.0-70.5°).

The infrared spectrum exhibited absorptions at 4.47 (CN), 7.87 (symmetrical epoxide stretch) and 11.30μ (asymmetrical epoxide stretch). The nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.67 (singlet, 10, aromatic) and 5.98 (singlet, 1, epoxide). The infrared and nmr spectra are recorded on pages 48 and 58.

trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile. A similar procedure was used for the preparation of this compound as for trans-2,3-diphenyl-2,3-epoxypropionitrile. To a solution of 41.6 g (0.19 moles) of trans- α -phenyl- β -p-tolylacrylonitrile in 240 ml of benzene cooled to 10°, 19.5 g of 90% tert-butylhydroperoxide was added slowly. Benzyltrimethylammonium hydroxide in methanol (Triton B) was concentrated under reduced pressure, and one and one-half milliliters were added to the benzene solution. The reaction mixture was placed in an ice bath and allowed to warm to room temperature overnight. The

benzene solution was washed with water, dried over magnesium sulfate, and concentrated to low volume under reduced pressure. The residue was recrystallized from methanol to give 37.0 g (84% yield) of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile. Further recrystallizations from a low volume of ether gave a product with a melting point of 81.0-81.5°.

The infrared spectrum exhibited absorptions at 4.47 (CN), 7.88 (symmetrical epoxide stretch), and 11.35 μ (asymmetrical epoxide stretch). The nmr spectrum (CCl₄, internal TMS) exhibited absorptions at τ 2.65 and 2.82 (multiplet, 9, aromatic), 6.05 (singlet, 1, epoxide), and 7.65 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 48 and 58.

Anal. Calcd. for C₁₆H₁₃NO: C, 81.65; H, 5.57.

Found: C, 81.67; H, 5.44.

trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile. The procedure for the preparation of this compound is the same as described for trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile. trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile was obtained when trans-2-phenyl-3-p-tolylacrylonitrile (24.1 g, 0.11 moles) was epoxidized with tert-butylhydroperoxide (13 ml, 90%) in the presence of benzyltrimethylammonium hydroxide (1.5 ml). After recrystallization from methyl alcohol, the product, 19.7 g (76%), was obtained. Further recrystallizations from a low volume of ether gave the product a melting point of 77.8-78.2°.

The infrared spectrum exhibited absorptions at 4.40 (CN), 7.90 (symmetrical epoxide stretch), and 11.45 μ (asymmetrical epoxide stretch). The nmr spectrum (CCl₄, internal TMS) exhibited absorptions at τ 2.60-2.90 (multiplet, 9, aromatic), 6.02 (singlet, 1, epoxide) and 7.68 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 48 and 58.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.65; H, 5.57.

Found: C, 81.77; H, 5.64.

Borontrifluoride Etherate Catalyzed Rearrangement of trans-2,3-Diphenyl-2,3-epoxypropionitrile. Borontrifluoride etherate (0.28 ml, 2.0 mmole) was added to a solution of 1.00 g (4.25 mmole) of trans-2,3-diphenyl-2,3-epoxypropionitrile in 13 ml of dry benzene and allowed to react for ten minutes. The benzene solution was then washed with water until the aqueous washings were barely acidic, dried ($CaCl_2$), and the solvent removed under reduced pressure yielding 0.99 g of crude product.

The infrared and nmr spectra of this sample indicated incomplete rearrangement of trans-2,3-diphenyl-2,3-epoxypropionitrile. The nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 0.45 (singlet, 0.37, aldehyde), 2.55-2.88 (multiplet, 10, aromatic), and 5.95 (singlet, 0.63, epoxide). The infrared spectrum exhibited absorptions at 4.45 (CN) and 5.77μ ($C=O$).

From the integrated nmr spectrum, unrearranged trans-2,3-diphenyl-2,3-epoxypropionitrile was present in 63% and α -cyanodiphenylacetonitrile was present in 37%.

Borontrifluoride Etherate Catalyzed Rearrangement of trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile. To a stirred solution of 2.09 g (8.5 mmole) of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile in 25 ml of dry benzene was added 0.55 ml (4.0 mmole) of freshly distilled borontrifluoride etherate. After ten minutes, the solution was washed with water until barely acidic, dried ($CaCl_2$) and filtered. A residue (2.04 g) was obtained after evaporation of solvent.

The nmr spectrum (CCl_4 , internal TMS) of this residue indicated complete rearrangement of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile and exhibited absorptions at τ 0.53 (singlet, 0.47, aldehyde), 2.70-2.95 (complex multiplet, 9, aromatic), 4.83 (singlet, 0.53, methyne), and 7.71 (doublet, 3, methyl).

Addition of deuterium oxide to the nmr sample resulted in no exchange with deuterium. The infrared spectrum exhibited two absorptions for a nitrile at 4.50 and 4.55 μ , and one absorption for a carbonyl at 5.85 μ .

If a sample of the epoxide was treated with borontrifluoride etherate in benzene (as above) but the benzene solution was evaporated under reduced pressure, a green residue was obtained which exhibited the same nmr spectrum as observed above. The infrared spectrum exhibited absorptions at 4.45, 4.50 (CN), and 5.75 μ (C=O). However, if the benzene solution was treated with a saturated solution of sodium bicarbonate in the work up procedure, the nmr spectrum remained identical except for the peak at τ 4.88 which disappeared. Addition of deuterium oxide resulted in no obvious change in the spectrum. The infrared spectrum exhibited a strong hydroxyl absorption at 3.14 μ .

The rearranged 2-phenyl-3-p-tolyl-2,3-epoxypropionitrile (1.09 g, 4.65 mmole) was chromatographed on neutral alumina, activity II-III. The evaporation of solvents gave only one fraction (petroleum ether-benzene) which solidified upon standing. The crystalline solid (0.40 g) was sublimed 60°/.05 mm), recrystallized from hexane, and resublimed, m.p. 61.0-62.0° (lit.²⁷ m.p. 61-62°). Molecular weight determination (CHCl_3) gave a molecular weight of 207. The infrared and nmr spectra of this compound were different than those observed for the rearranged epoxide, but were in accord with the structure of phenyl-p-tolylacetonitrile. The nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.75 (singlet, 5, aromatic), 2.90 (singlet, 4, aromatic), 5.05 (singlet, 1, methyne), and 7.70 (singlet, 3, methyl). The infrared spectrum exhibited a nitrile absorption at 4.48 μ . The spectra are recorded on pages 50 and 60.

Utilizing the method of Shine⁴⁷ for the preparation of 2,4-dinitrophenylhydrazones, 0.50 g (2.13 mmole) of rearrangement product from trans-2-phenyl-

3-p-tolyl-2,3-epoxypropionitrile was added to 13 ml of a 0.168 M solution of 2,4-dinitrophenylhydrazine (2.18 mmole) in diglyme followed by three drops of concentrated hydrochloric acid. Evaporation of the solvent under reduced pressure left a bright yellow-red residue. Fractional recrystallization from ethanol-ethyl acetate gave a difficult to purify residue and excess 2,4-dinitrophenylhydrazine. No other 2,4-dinitrophenylhydrazone could be isolated.

Repeating the above procedure using 7 ml (1.17 mmole) of 2,4-dinitrophenylhydrazine reagent in place of the 13 ml, 0.36 g (41% yield) of the 2,4-dinitrophenylhydrazone was obtained after recrystallization from ethanol-ethyl acetate. Repeated recrystallization from ethanol-ethyl acetate gave an analytical sample of m.p. 178-178.5°.

The infrared and nmr spectra indicated the product to be α-cyanophenyl-p-tolylacetaldehyde 2,4-dinitrophenylhydrazone. The nmr spectrum (CDCl₃) exhibited peaks at τ -1.15 (broad singlet, 1, NH), 0.19 (doublet, 1, aromatic), 1.6-1.8 (quartet, 1, aromatic), 1.82 (singlet, 1, aromatic), 2.10 (singlet, 1, aldehyde), 2.57 (singlet, 5, aromatic), 2.73 (singlet, 4, aromatic) and 7.63 (singlet, 3, methyl). The infrared spectrum exhibited absorptions at 3.09 (m, NH), 4.46 (vw, CN) and 6.20 μ (s, C=N).

Anal. Calcd. for C₂₂H₁₇N₄O₄: C, 63.61; H, 4.13; N, 16.86.

Found: C, 63.86; H, 4.02; N, 16.93.

Two grams (8.50 mmole) of the rearrangement product of trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile in 50 ml of ether was extracted three times with 5% aqueous potassium carbonate. The ether layer was washed with water, and the water was added to the carbonate extracts. The ethereal solution was dried (CaCl₂) and then evaporated to yield 1.0 g of α-cyanophenyl-p-tolylacetaldehyde, and phenyl-p-tolylacetonitrile. The mixture was chromatographed on neutral alumina, activity II-III. Elution with and evaporation of

methylene chloride gave 0.80 g of phenyl-p-tolylacetonitrile. The product was sublimed at $60^{\circ}/0.05$ mm, m.p. $59-60^{\circ}$ (lit.²⁷ $61-62^{\circ}$) and the recovery was 45.5%.

The nmr spectrum was identical to that previously recorded for phenyl-p-tolylacetonitrile on pages 50 and 60.

The potassium carbonate solution was cooled with ice, and acidified immediately with 10% hydrochloric acid. The acidified solution was extracted three times with ether, saturated with sodium chloride, and extracted again with ether. The ether extracts were combined, washed with water, and dried (CaCl_2). Evaporation of the ether left an oil (1.0 g) which solidified on addition of carbon tetrachloride. Recrystallization from cyclohexane gave 0.64 g of product, m.p. $111-112^{\circ}$ (sealed tube). A sample was taken and purified further by slow sublimation at $70^{\circ}/0.05$ mm followed by two recrystallizations from cyclohexane, m.p. $114-115^{\circ}$ (sealed tube). An nmr spectrum of the sample indicated no change in purity. The product was resublimed and submitted for analysis.

Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{NO}$: C, 81.68; H, 5.57.

Found: C, 81.27; H, 5.64.

The infrared and nmr spectra shown on pages 52 and 62 indicate the presence of an enol. The infrared spectrum (KBr) exhibited absorptions at 3.09μ for the enol and 4.50μ for the nitrile. The infrared spectrum in chloroform (15%) gave a similar spectrum; 4.53 (CN), and $2.90-3.10\mu$ (broad OH). The nmr spectrum (CDCl_3 , internal TMS) exhibited a broad absorption at $\tau 4.05$ (1, hydroxyl) which disappeared on addition of deuterium oxide, in addition to the absorption at 2.70 and 2.85 (multiplet, 9, aromatic), and 7.68 (doublet, 3, methyl). The ultraviolet spectrum of this compound exhibited absorption maxima, in ethanol, at 290 ($\log \epsilon$, 4.23) and 235 $m\mu$ ($\log \epsilon$, 4.08). The ultra-

violet spectrum is shown on page 68. The mass spectrum showed a loss of 54 m/e (COCN) and 27 m/e (HCN) from the parent ion (235 m/e). The bar graph of the mass spectrum is shown on page 66. The above spectral data indicated that the product was α -hydroxy- β -phenyl- β -p-tolylacrylonitrile.

Two grams of the rearrangement product from trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile was dissolved in 15 ml of 95% ethanol, and 17 ml of a 5% solution of potassium carbonate was added to the solution. The solution was stirred for one hour then diluted with water and extracted with ether. The combined ether extracts were washed with water, dried (MgSO_4), and excess ether evaporated. The nmr spectrum of the residue (1.4 g) indicated phenyl-p-tolylacetonitrile to be present, and another compound which exhibited similar absorptions, which has never been isolated before. The residue was not further investigated.

The potassium carbonate solution was cooled with ice, acidified with 10% hydrochloric acid, and extracted with ether. The combined ether extracts were washed with water, dried (MgSO_4), and excess ether evaporated leaving a residue (0.46 g) which soon solidified. Recrystallization from cyclohexane gave 0.27 g of phenyl-p-tolylacetic acid, m.p. 116-117° (lit.²⁶ m.p. 115-116°).

The infrared spectrum exhibited absorptions at 3.40 (OH) and 5.85 μ (CO). The nmr spectrum (CDCl_3 , internal standard) exhibited absorptions at τ -1.85 (broad singlet, 1, acid), 2.73 and 2.85 (multiplet, 9, aromatic), 5.00 (singlet, 1, methyne), 7.70 (singlet, 3, methyl). The infrared and nmr spectra, recorded on pages 50 and 60, indicated this product to be phenyl-p-tolylacetic acid.

Borontrifluoride Etherate Catalyzed Rearrangement of trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile. To a stirred solution of 2.03 g (8.5 mmole) of trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile in 25 ml of dry benzene was added

0.55 ml (4.0 mmole) of freshly distilled borontrifluoride etherate. After ten minutes, the solution was washed with water until barely acidic, dried (CaCl_2), and filtered. An oil (1.99 g) was obtained after evaporation of excess benzene. The nmr spectrum (CCl_4 , internal TMS) of this oil indicated complete rearrangement of the trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile. Absorptions at ν 0.48 (singlet, 1, aldehyde) were observed, along with the peaks at 2.68 (triplet, 5, aromatic), 2.87 (singlet, 4, aromatic) and 7.67 (singlet, 3, methyl). The infrared spectrum exhibited absorptions at 4.45 ($-\text{CN}$) and 5.75μ ($-\text{CO}$).

The oil (0.20 g, 0.85 mmole) was chromatographed on neutral alumina, activity II-III. Evaporation of the solvents gave only one fraction (CCl_4 -benzene). The oil obtained (0.16 g) solidified upon standing. The product was sublimed at $60^\circ/0.05$ mm to give the product (92%) with a melting point of $60-61^\circ$. The infrared and nmr spectra were identical to those previously obtained for phenyl-p-tolylacetonitrile, pages 50 and 60.

The preparation of the 2,4-dinitrophenylhydrazone was similar to that of the trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile rearranged products. A sample (0.50 g, 2.13 mmole) of previously rearranged trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile was added to 15 ml of a 0.168 M solution of 2,4-dinitrophenylhydrazine in diglyme followed by 3 drops of concentrated hydrochloric acid. The solution was cooled, and a residue formed on addition of water. Recrystallization from ethanol-ethyl acetate gave 0.48 g (55%) of the 2,4-dinitrophenylhydrazone, m.p. $178.0-178.5^\circ$. The infrared and nmr spectra were identical to that of g-cyanophenyl-p-tolylacetaldehyde 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_4\text{O}_4$: C, 63.61; H, 4.13; N, 16.86.

Found: C, 63.54; H, 4.01; N, 16.78.

Two grams (8.5 mmole) of rearranged epoxide were dissolved in ether and treated with a 5% solution of potassium carbonate. The ether layer was washed, dried, and ether evaporated under reduced pressure. An nmr spectrum of the oil remaining indicated a mixture of phenyl-p-tolylacetonitrile and α-cyano-phenyl-p-tolylacetaldehyde. The oil was chromatographed on neutral alumina, activity II-III, and eluted with methylene chloride. Evaporation of the solvent gave 1.6 g (7.75 mmole) of phenyl-p-tolylacetonitrile (91%). Sublimation at 60°/0.05 mm gave the product with a melting point of 61-62°. The nmr spectrum was identical to that of phenyl-p-tolylacetonitrile recorded on page 60.

The potassium carbonate solution was cooled and acidified with 10% hydrochloric acid followed by extraction with ether. The combined ether extracts were washed, dried (CaCl_2), and the solvent was removed leaving a residue (2 mg) which was not further investigated.

Purification of α-cyanophenyl-p-tolylacetaldehyde was difficult due to the ease of decarbonylation in the presence of base. Attempted bisulfite addition and distillation also resulted in quantitative yields of phenyl-p-tolylacetonitrile. If the crude aldehyde was dissolved in benzene, washed once with a saturated solution of sodium bicarbonate followed with water, dried, and solvent evaporated, the purest α-cyanophenyl-p-tolylacetaldehyde was obtained.

The infrared spectrum exhibited absorptions at 4.45 (CN), and 4.75 μ (C=O). The nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at 7.045 (singlet, 1, aldehyde), 2.72 (triplet, 5, aromatic), 2.68 (singlet, 4, aromatic), and 7.67 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 50 and 60.

Phenyl-p-tolylacetonitrile. To a solution of silver nitrate in ammonia

(Tollens' reagent) was added 0.75 g (3.2 mmole) of α -cyanophenyl-p-tolylacet-aldehyde (obtained directly from the borontrifluoride etherate rearrangement of trans-3-phenyl-2-p-tolyl-2,3-epoxypropionitrile). The silver precipitate formed was filtered off, washed with hot water and methanol, and the filtrate acidified. The solution was cooled, filtered, and the crystals obtained were sublimed at 60°/.05 mm giving 0.43 g (65%) of phenyl-p-tolylacetonitrile, m.p. 60-61° (lit.²⁷ m.p. 60-61°).

The nmr and infrared spectra for this compound are identical to the spectra obtained from the chromatography of both rearranged epoxides. The spectra are recorded on pages 50 and 60.

Phenyl-p-tolylacetamide. Phenyl-p-tolylacetonitrile (0.40 g, 1.93 mmole) was hydrolyzed in 10 ml of 75% sulfuric acid at 100° for eleven hours. The cooled solution was poured over ice and extracted with ether. The ether layers were combined, extracted three times with a 5% solution of potassium carbonate, and washed with water. The ethereal solution was dried and excess solvent removed leaving a crystalline product (0.14 g). The infrared and nmr spectra indicated the product to be phenyl-p-tolylacetamide, m.p. 155.7-156° (lit.⁵⁹ 151°). The infrared spectrum exhibited an absorption for the carbonyl at 6.05 μ and an absorption at 3.02 μ for the NH₂. The nmr spectrum (CDCl₃, internal TMS) exhibited absorptions at τ 2.75 (singlet, 5, aromatic), 2.88 (singlet, 4, aromatic), 3.70-4.50 (broad singlet, 2, NH₂), 5.13 (singlet, 1, methyne), and 7.70 (singlet, 3, methyl).

Hydrolysis of α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile.

1. With Aqueous Sulfuric Acid (25%). α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile (0.20 g, 0.89 mmole) was hydrolyzed in 10 ml of 25% aqueous sulfuric acid at 100° for six hours. The solution was cooled and extracted with ether. The combined ether extracts were extracted with 5% aqueous

potassium carbonate and washed with water. Evaporation of the ether layer left a residue (2 mg) which was not further investigated. After acidification of the carbonate extracts with 10% hydrochloric acid and extraction with ether, the ether layer was washed with water, dried (CaCl_2), and evaporated to yield 0.14 g of an oil which soon solidified. Recrystallization from cyclohexane gave .09 g (45%) of phenyl- β -tolylacetic acid, m.p. 114.5-115° (lit.²⁶ m.p. 115-116°). The infrared and nmr spectra obtained were identical to that obtained previously for phenyl- β -tolylacetic acid. The spectra are recorded on pages 50 and 60.

2. With 5% Aqueous Sodium Hydroxide. α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile (0.20 g, 0.89 mmole) was also hydrolyzed with 10 ml of 5% aqueous sodium hydroxide at 100° for six hours. After the cooled solution was extracted with ether, the basic solution was acidified with 10% sulfuric acid, and extracted again with ether. The ether extracts of the acidified solution were combined, washed, dried, and excess solvent evaporated. The solid obtained (0.17 g) was recrystallized from cyclohexane to yield 0.16 g (80% yield) of phenyl- β -tolylacetic acid, m.p. 114-115° (lit.²⁶ m.p. 115-116°). The infrared and nmr spectra were identical to those obtained for phenyl- β -tolylacetic acid. The spectra are recorded on pages 50 and 60.

α -Methoxy- β -phenyl- β -p-tolylacrylonitrile. An excess of diazo methane (2.0 mmole) was added to 0.30 g (1.28 mmole) of α -hydroxy- β -phenyl- β -p-tolylacrylonitrile in ether. After three hours, the excess diazomethane and ether were removed under vacuum to obtain an oil whose nmr spectrum indicated a good yield of the methyl vinyl ether. The oil was taken up in ether and extracted with a dilute solution of sodium bicarbonate to rid the solution of any enol that might be present. The solid obtained upon evaporation of ether was sublimed three times (60°/0.05 mm) and recrystallized twice from pentane inter-

changeably until the product appeared pure from the nmr spectrum. An analytical sample (0.05 g) of α -methoxy- β -phenyl- β -p-tolylacrylonitrile was obtained, m.p. 79.5-80.5°. The infrared spectrum exhibited a nitrile absorption at 4.58μ . The nmr spectrum (CCl_4 , internal TMS) exhibited absorptions at τ 2.73 (singlet, 5, aromatic), 2.94 (multiplet, 4, aromatic), 6.26 (singlet, 3, methoxy), and 7.70 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 52 and 62, and are in accord with the assigned structure.

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{NO}$: C, 81.91; H, 6.07.

Found: C, 82.01; H, 6.08.

α -Cyanodeoxybenzoin. A similar procedure to that employed by Kohler and Blatt²² was used for the preparation of this compound. To a well stirred solution of 6.1 g (0.10 moles) of a 40% sodium hydride dispersion in 50 ml of dry ether, 5.84 g (0.05 moles) of phenylacetonitrile was added dropwise. The ethereal solution was heated under reflux for 0.5 hour, cooled and ethyl benzoate (7.50 g, .05 moles) was added dropwise to the solution. The resultant solution was stirred overnight, then was hydrolyzed by the slow addition of water, and extracted with ether. The aqueous layer was cooled, acidified (10% H_2SO_4), and extracted with ether. The combined ether extracts were washed, dried (CaCl_2), filtered, and ether removed under reduced pressure. α -Cyanodeoxybenzoin (7.9 g) was recrystallized from ether-cyclohexane to give 7.0 g (64%) of product, m.p. 91.5-92.0° (lit.⁵⁶ m.p. 91-92°).

The infrared spectrum exhibited absorptions at 4.47 (CN), and 5.95μ (CO). The nmr spectrum (CDCl_3 , internal TMS) exhibited absorptions at τ 1.95-2.18 and 2.40-2.85 (complex multiplets, 9, aromatic) and 4.33 (singlet, 1, methyne). The infrared and nmr spectra are recorded on pages 54 and 64. Addition of deuterium oxide resulted in no exchange with deuterium. The ultraviolet spectrum, similar to that reported by Russell,³⁹ exhibited absorption

maxima at 291 ($\log \epsilon$ 4.12) and 249 $m\mu$ ($\log \epsilon$ 3.97) in ethanol.

α -Cyano-4'-methyldeoxybenzoin. The preparation of this compound is similar to that of α -cyanodeoxybenzoin. Phenylacetonitrile (5.84 g, 0.05 moles) was added dropwise to a well stirred solution of 6.1 g (0.10 moles) of a 40% sodium hydride dispersion in 60 ml of dry ether, and the resultant solution was heated for 0.5 hour. After cooling, 7.50 g (0.50 moles) of methyl toluate was added dropwise to the reaction mixture. Since no noticeable reaction had occurred after ten hours, the reaction mixture was heated for twenty-four hours. The cooled solution was hydrolyzed by the slow addition of water, and the resultant solution was extracted with ether. The aqueous solution was acidified with 10% sulfuric acid and extracted with ether. The ether extracts were combined, washed with water, dried (CaCl_2), filtered, and the ether was evaporated under reduced pressure. The oil obtained solidified upon standing. Recrystallization from ether-cyclohexane gave 7.7 g (66%) of α -cyano-4'-methyldeoxybenzoin, m.p. 104.0-104.5°.

The infrared spectrum exhibited absorptions at 4.45 (CN) and 5.97 μ (C=O). The nmr spectrum (CDCl_3 , internal TMS) exhibited absorptions at τ 2.05-2.30 and 2.50-2.90 (complex multiplets, 9, aromatic), 4.37 (singlet, 1, methyne) and 7.65 (singlet, 3, methyl). The infrared and nmr spectra of α -cyano-4'-methyldeoxybenzoin are shown on pages 54 and 64. Addition of deuterium oxide resulted in no exchange with deuterium. The ultraviolet spectrum in ethanol exhibited an absorption maximum at 290 $m\mu$ ($\log \epsilon$ 4.12).

Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{NO}$: C, 81.68; H, 5.57.

Found: C, 82.23; H, 5.50.

α -Cyano-4'-methyldeoxybenzoin. The method of preparation of this compound is the same as for α -cyano-4'-methyldeoxybenzoin except p-tolylacetonitrile was condensed with ethyl benzoate in the presence of sodium hydride to give

α -cyano-4-methyldeoxybenzoin. Recrystallization from ether-cyclohexane gave 9.5 g (81%) of product, m.p. 94.0-94.5°.

The infrared spectrum exhibited absorptions at 4.48 (CN), and 5.95 μ (CO). The nmr spectrum (CDCl₃, internal TMS) exhibited absorptions at τ 1.95-2.17 and 2.42-2.97 (complex multiplets, 9, aromatic), 4.37 (singlet, 1, methyne) and 7.73 (singlet, 3, methyl). The infrared and nmr spectra are recorded on pages 54 and 64. Addition of deuterium oxide resulted in no exchange with deuterium. The ultraviolet spectrum in ethanol exhibited an absorption maximum at 293 m μ (log ϵ 4.14).

Anal. Calcd. for C₁₆H₁₃NO: C, 81.68; H, 5.57.

Found: C, 82.15; H, 5.48.

Acidic Hydrolysis of α -Cyano-4-methyldeoxybenzoin. This compound was hydrolyzed under the same conditions as α -hydroxy- β -phenyl- β -p-tolylacrylonitrile. α -Cyano-4-methyldeoxybenzoin (0.30 g, 1.34 mmole) was hydrolyzed with 10 ml of 25% aqueous sulfuric acid at 100° for six hours. The acidic solution was extracted with ether, and the combined ether extracts were washed with water, dried, and the ether was evaporated. An nmr spectrum of the solid obtained indicated the hydrolysis was incomplete.

The above procedure was repeated with 50% sulfuric acid for eight hours at 115°. The acidic solution was diluted with cold water, and extracted with ether. The ether extracts were combined and extracted with a 10% solution of sodium hydroxide to remove the excess α -cyano-4-methyldeoxybenzoin. The ether layer was washed with water, dried, and the solvent evaporated. A residue (0.13 g) obtained was recrystallized from ethanol to give 0.08 g of 4-methyldeoxybenzoin, m.p. 95.0-95.5° (lit.⁵¹ m.p. 94°).

The nmr spectrum (CCl₄, internal TMS) exhibited absorptions at 2.00-2.32 and 2.48-2.75 (complex multiplet, 5, aromatic), 2.95 (singlet 4,

aromatic), 5.90 (singlet, 2, methylene) and 7.73 (singlet, 3, methyl). The nmr spectrum of this sample is in accord with 4-methyldeoxybenzoin.

Borontrifluoride Etherate Treatment of α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile. α -Hydroxy- β -phenyl- β -p-tolylacrylonitrile (20 mg) was dissolved in 5 ml of dry benzene followed by the addition of four drops of borontrifluoride etherate. The reaction mixture was stirred for 0.5 hour, then was washed, dried, and excess benzene evaporated. The residue obtained (20 mg) solidified upon standing. The nmr spectrum indicated this product to be unreacted α -hydroxy- β -phenyl- β -p-tolylacrylonitrile.

Borontrifluoride Etherate Treatment of α -Cyano-4-methyldeoxybenzoin. α -Cyano-4-methyldeoxybenzoin (0.50 g, 2.13 mmole) was dissolved in 25 ml of dry benzene and treated with 0.50 ml borontrifluoride etherate. After 15 minutes, the benzene solution was washed, dried, and excess benzene evaporated to give 0.48 g of crystalline solid. An identical nmr spectrum to that of α -cyano-4-methyldeoxybenzoin was obtained.

Attempted Preparation of α,α -Diphenylpyruvonitrile.

1. Neat. Phosphorus tribromide (1.5 ml) was added to a solution of 2.00 g (9.45 mmole) of diphenylacetic acid in 10 ml of benzene. The solution was heated under reflux for two hours. The benzene solution was separated from the phosphorous acid residue, and excess benzene evaporated. An nmr spectrum of the oil obtained indicated the acid bromide to be present in about 85%.

A similar procedure to that described for the preparation of benzoyl cyanide was used for the attempted preparation of α,α -diphenylpyruvonitrile.³² The freshly prepared acyl bromide was heated (neat) with 1.0 g of dry cuprous cyanide at 120° for two hours. The tar obtained was only partially soluble in benzene. An nmr spectrum of this tar indicated no desired products; therefore

it was not further investigated.

2. In Benzene at 75°. The alternate method of preparation of this compound is similar to that described by Schreiber.⁴⁵ Diphenylacetyl bromide was prepared (as above) and added dropwise to a benzene solution containing 1.1 g of dry cuprous cyanide. The resultant solution was heated to 75° for two hours. The dark brown solution was then cooled, washed with water, dried, and excess solvent evaporated. The infrared spectrum indicated the acyl cyanide was present, but only in low yield. Absorptions were observed at 4.51 μ (CN) and 5.85 μ (C=O) for the acyl cyanide. An absorption was also observed at 5.55 μ indicating a large amount of acyl bromide still present. The preparation of this compound was not further investigated.

Neat Thermal Rearrangement of trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile. trans-2-Phenyl-3-p-tolyl-2,3-epoxypropionitrile (2.0 g, 8.6 mmole) was heated at 200° under full vacuum and passed successively through a 200 mm column, heated to 350° by a coil furnace. The temperature was measured by a thermocouple. The rearrangement was followed by nmr spectroscopy.

<u>Times Through Column</u>	<u>% Rearranged</u>
1	11%
3	27%
4	30%

Since the rearrangement of the epoxide was proceeding at a slower rate, the crystalline material was recrystallized from methanol to remove some of the epoxide (0.43 g). The residue obtained was chromatographed on neutral alumina, activity II-III. Elution with cyclohexane-carbon tetrachloride gave 0.61 g recovered epoxide, 0.52 g of a mixture of epoxide and rearranged product, and 0.14 g of thermally rearranged product. Three successive sublimations gave 0.12 g of pure rearranged epoxide, m.p. 85.5-86°.

The infrared and nmr spectra indicated the product to be cis-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile. The infrared spectrum exhibited absorption at 4.45μ (CN). Other bands present at 8.48 and 11.13μ could be attributed to the symmetric and asymmetric stretch of the epoxide ring.^{2,31} The nmr spectrum (CCl_4 , internal TMS) exhibited peaks at τ 2.70 (singlet, 5, aromatic), 3.00 (singlet, 4, aromatic), 5.32 (singlet, 1, epoxide), and 7.77 (singlet, 3, methyl).

Neat Thermal Rearrangement of trans-3-Phenyl-2-p-tolyl-2,3-epoxypropionitrile.

The procedure for the thermal rearrangement of this compound was the same as for trans-2-phenyl-3-p-tolyl-2,3-epoxypropionitrile. The per cent of rearranged product, as determined by nmr spectroscopy, is given as follows.

<u>Times Through Column</u>	<u>% Rearranged</u>
1	11%
2	20%
3	28%
4	30%

It was concluded that trans to cis isomerization must be occurring also for this compound; therefore, the rearrangement was not further investigated.

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STUDIES IN THE EPOXIDE-CARBONYL
REARRANGEMENT OF α -CYANO EPOXIDES

by

DONALD G. HILL

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ABSTRACT

The syntheses and the borontrifluoride etherate catalyzed rearrangements of trans-2,3-diphenyl-2,3-epoxypropionitrile (5a), trans-2-phenyl-3-*p*-tolyl-2,3-epoxypropionitrile (5b), and trans-3-phenyl-2-*p*-tolyl-2,3-epoxypropionitrile (5c) are described. The syntheses of 5a, 5b, and 5c were accomplished by the treatment of trans- α , β -diphenylacrylonitrile (35a), trans- α -phenyl- β -*p*-tolylacrylonitrile (35b), and trans- β -phenyl- α -*p*-tolylacrylonitrile (35c) with tert-butylhydroperoxide in the presence of benzytrimethylammonium hydroxide.

The borontrifluoride etherate catalyzed rearrangements of the α -cyano epoxides, 5a, 5b, and 5c, in benzene resulted in formation of α -cyanodiphenylacetaldehyde (107, 37%), α -cyanophenyl-*p*-tolylacetaldehyde (89, 47%) and phenyl-*p*-tolylpyruvonnitrile (90, 53%), and 89 (100%), respectively, by phenyl or *p*-tolyl migration. The products observed are explained by the formation of the most stable carbonium ion by a stepwise mechanism. The stereochemistry of the transition state would be nearly identical for a concerted process and, therefore, would not be a determining factor in the ratios of products observed.

The thermal rearrangements of 5b and 5c were also observed, but only resulted in the trans to cis isomerizations.